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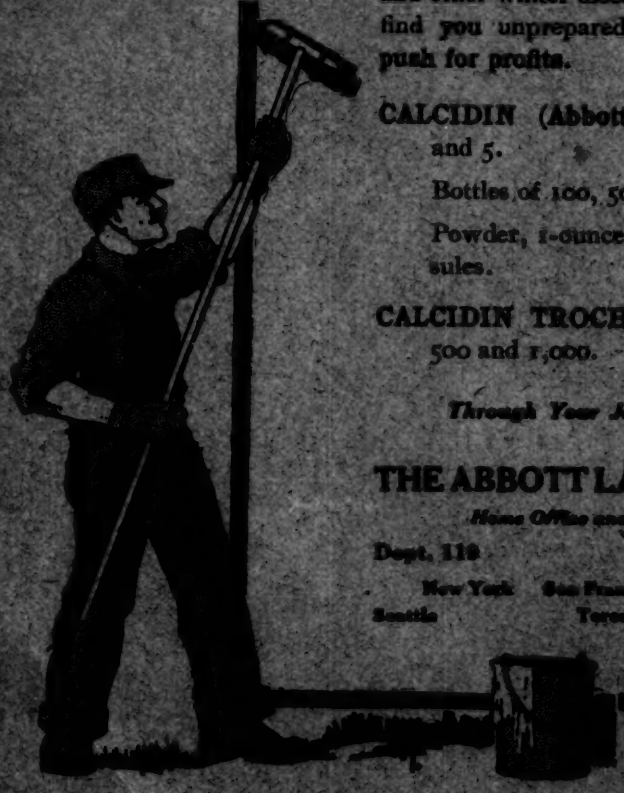

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THE AMERICAN
JOURNAL OF PHARMACY

NOVEMBER, 1919

EDITORIAL.

PHARMACISTS AND THE PROHIBITION ENFORCEMENT LAW.

The National Prohibition Enforcement Act and the regulations (T. D. 2940) issued by the Internal Revenue Bureau for the enforcement of this and the several Congressional enactments that were precursory thereto, have placed additional responsibilities upon the pharmacists of the United States. In anticipation of such action, the former president of the American Pharmaceutical Association recommended at the New York meeting that such added responsibilities "should be accepted as a tribute to the dignity and responsibility of the calling and as a recognition of the honesty and worthiness of the profession as a whole which is implied by such a trust." We have faith in the medical and pharmaceutical professions and believe that these on the whole will measure up fully to the responsibility.

Whatever the reasoning that actuated the framers of this law, its enactment has established beyond controversy several important principles. The use of distilled spirits and wines as medicines is clearly recognized as a proper use of non-beverage liquors and thus the limitations of T. D. 2788 which declared "that the withdrawal of whiskey, brandy, and other distilled spirits was presumed to be for *beverage purposes*" and not permissible under the War Prohibition Law and the further declaration therein that "it is not believed that there is any legitimate use for wines for medicinal purposes" are abrogated. Other distilled spirits for medicinal purposes, as well as alcohol, is thereby made available at the non-beverage excise tax of $2.20 per proof gallon instead of the bever-

age spirit tax of $6.40, and likewise vinous spirits that are prescribed as medicines or as vehicles for medicines.

The law very rightly now recognizes these "liquors" as medicinal substances to be prescribed only by a physician who holds a permit to prescribe liquors and is duly licensed to practice medicine and actively engaged in the practice of such profession, and in good faith as a medicine after a careful examination of the person for whom the liquor is prescribed. In the future such prescriptions will, except in certain emergencies, have to be written on official forms supplied by the commissioner, serially numbered and with stubs on which copies of the prescriptions are to be kept and returned to the commissioner. Not more than a pint of spirituous liquor to be taken internally shall be prescribed for use by the same person within any period of ten days and no such prescription shall be filled more than once.

The compounding of these prescriptions must be by a pharmacist who has a permit under the Act and "who is duly licensed under the laws of his state to compound and dispense medicine." Here we have a Congressional recognition of the licensed pharmacist as the only person to compound and dispense medicine, a principle for which pharmacists have long contended.

While the enforcement of this law is left with the Treasury Department and its Bureau of Internal Revenue, it is apparent that it is no longer merely a question of revenue collection that is concerned. This Department has all the machinery necessary and many years of experience and many officials and employees trained in the methods of the distilling and wine industries and so the framing of regulations and the carrying into effect the provisions of the National Prohibition Act has been made a special feature and duty of the Commissioner of Internal Revenue, and it is understood that a new division composed of Federal Prohibition Enforcement Officers is to be created.

With the changes which time, education, and the advanced moral tone of our people have effected, the "liquor business" as a merchandising of alcoholic beverages is a thing of the past and the "liquor dealer" has ceased to exist. This law does not mention such, but makes it a part of the professional duty of the pharmacist to dispense alcoholic medicines in accordance with regulations which minimize the possibility of the infraction of the law. It also recog-

nizes that alcohol is indispensable in the preparation and preservation of many medicines. The dispensing of distilled and vinous liquors as medicines is thus recognized as a distinctly professional duty of the pharmacists and of no other class and as a necessary non-beverage use of these. It would follow that the necessity for the classification of "Retail Liquor Dealer" had ceased to exist in the Treasury Department. The pharmacist under this permit can never become a dealer in or dispenser of beverage spirits and his classification under this objectionable title is now, more than ever before, incongruous and should be forthwith discontinued by direction of the Department as inconsistent with the law and the regulations.

The regulations, T. D. 2940, that have been framed by the Department for the enforcement of the National Prohibition Act and the several preceding acts known as the Food Control Act, the War Prohibition Act and the Revenue Law of 1918 contain many features that will have to be carefully studied by pharmacists in order that they may comply therewith. As we now view these, it would seem that it may prove a hardship if not impracticable to literally comply with some of the most exacting.

All persons who desire to use for manufacturing purposes or to sell distilled spirits or wines for medicinal or non-beverage purposes will be required to file an application in triplicate with the Prohibition Enforcement Officer of the State in which the business is to be conducted which must be approved by the Commissioner of Internal Revenue and likewise a bond in duplicate to be approved by the said Prohibition Enforcement Officer. The minimum amount of the bond is to be $1,000, the maximum $100,000 in accordance with quantity of liquors purchased. All permits issued prior to November, 1919, will have to be renewed under the amended form and the permit must receive the approval of the Commissioner and all holders of these permits are required to give a new bond not later than December 1, 1919.

The new form of application for permit contains several new features. Paragraph (*b*) in this provides for a statement regarding each preparation that is neither U. S. P. or N. F., requiring the name of the preparation, for whom manufactured, per cent. of alcohol by volume, and each of these preparations must have the approval of the Commissioner. When new special formulas or preparations are

manufactured in excess of five gallons within a period of 90 days, a separate or supplemental permit must be obtained. The formula and process of each of these non-official preparations, upon request, are to be furnished the Commissioner for approval before permit is approved. This provision will be somewhat of a hardship to the manufacturing pharmaceutical houses who list a long line of unofficial fluid extracts, tinctures, elixirs and specialties made either for their own sales or very frequently as private formulas for druggists, physicians, or for proprietary medicine dealers.

A duly licensed practitioner of medicine may secure a permit without giving bond for the purchase of not exceeding two quarts of alcohol or alcoholic preparations during a period of one year by filing the required application for permit and making sworn statement that such alcohol or alcoholic preparations are to be used in his practice. This is probably a concession to the homeopathic physicians who objected to the limitations placed upon the procuring of their tinctures and alcoholic dilutions under the regulations of T. D. 2788.

The law, under Title II, Section 4, states that medicinal preparations made in accordance with the formulas of the American Institute of Homeopathy that are unfit for beverage purposes, "shall not be subject to the provisions of this Act." Evidently the intent was to recognize the Homeopathic Pharmacopoeia of the United States, prepared by a committee of that body and published by the Institute, as the official authority for homeopathic remedies. The mention thus made in the same sentence as are named the United States Pharmacopoeia and the National Formulary would indicate that a standing or recognition of these three as coequal as standards for the formulas contained was what was intended by the law. Under these conditions it is rather singular that the regulations fail to mention the Homeopathic Pharmacopœia or to make any reservations concerning the medicines used especially by that school.

It is noteworthy that in these proposed regulations the Department has promulgated standards for alcoholic preparations in which non-beverage alcohol may be used. Paragraph (*a*) of these states that "U. S. P. and N. F. preparations, except such as may be designated by the Commissioner as suitable for use as a beverage or which have no legitimate use as a vehicle." This certainly places

rather remarkable responsibility and assumption of authority upon the Commissioner, who presumably is not a medical man, to determine what the medical practitioners of the country shall be permitted to prescribe as remedial agents or as vehicles for such remedies. The scope of the Pharmacopœia is limited solely to substances and formulas "which are used for medicinal purposes," and the judgment of the Committee of Revision composed of practitioners and scientific workers in this special field, should not be set aside by the precipitate opinion of an official.

Paragraph (*b*) of these standards attempts to define a ***medicine*** under this law, that term not being defined in the Act itself. The definition given is: "(*b*) Any medicinal preparation will be classed as a medicine, provided the same is unfit for use as a beverage, and contains no more alcohol than is necessary for the purpose of extraction, solution or preservation, and contains in each fluid ounce a dose as a whole or in compatible combination of one or more agents of recognized therapeutic value, and contains no agents either chemically or physiologically incompatible with the active medicinal agents upon which the medicinal claims are based." The wording of this paragraph is unfortunate. The adjective "medicinal" applied to a preparation stamps such as having the properties and uses of a medicine. A "medicinal preparation" is incontrovertibly a "medicine" and a declaration of a department cannot change its status. A medicine is a medicine as much as "pigs are pigs."

Again who is to determine which of the "agents" are "of recognized therapeutic value"? There is a wide diversity of opinion among able medical practitioners as to "therapeutic value" of many of the remedial agents that are extensively employed and where the doctors differ among themselves would it be safe to accept the dictum of a non-medical department? In a "compatible combination" may not even the alcohol contained be one of the "agents of recognized therapeutic value"?

When we stop to consider the innumerable chemical and physiological incompatibilities possible and the many times that either accidentally or intentionally these are evidenced in the prescriptions of the most learned and skilled physicians we must conclude that the department is promulgating an impracticability bordering on the verge of the ridiculous and which must, necessarily, be observed

very frequently in the breach. In this paragraph, in assuming authority to interpret the propriety of medical customs and practices, the Department is treading upon dangerous ground in which, for the welfare of the people, it would be well not to be too aggressive.

In the establishing in this portion of the regulations definitions and standards for flavoring extracts, the Bureau of Internal Revenue is taking another advanced step and one which, when the Food and Drugs Act was under consideration, Congress declined to sanction. The attitude of Congress at that time was that the duty of a Department of the Government was administrative, to enforce the laws, and not to make them; that a department should not be given the authority to make the standards for the articles of food and drug consumption which it was to be entrusted to pass upon in its enforcement of the law; that it should not be empowered thus to act in the dual capacity of law maker and enforcer. It is an open question whether public opinion and legislative sentiment have since changed to warrant now the departure from that attitude.

A flavoring extract is defined "as a solution, in ethyl alcohol of *proper* strength, of the sapid and odorous principles derived from an aromatic plant, with or without its coloring matter, and conforms in name to the plant used in its preparation." It is to be observed that if any coloring is used in these preparations it must be the natural coloring matter of the plant named. This eliminates the use in these of artificial coloring of any kind or character. Standards are named for twenty-three flavoring extracts, a differentiation being made between extracts of cassia and cinnamon and between anise and star anise extracts. Tincture of ginger is held to be a "medicinal preparation" and not a flavoring extract and must be made according to the U. S. P. and no standard is given for ginger extract.

The enormity of the task that has been placed upon the Internal Revenue to enforce the recently enacted Narcotic and Prohibition Laws, which are more police measures than they are treasury enactments, calls for our sympathy and coöperation and our criticisms are intended as constructive aids. It is likewise the duty of the medical and pharmaceutical professions to assist faithfully, not only in the discharge of the responsibility placed upon them by these enactments, but also to sustain and uphold the spirit of these laws and to

support the officials in their enforcement. Nevertheless Congress in its lawmaking and the Departments in the framing of regulations should obtain the advice of the professions or trade interests that are directly concerned. If this co-operation was sought and advice accepted many of the inconsistencies could be avoided. The legislation and the regulations here commented upon are practical illustrations of the impracticabilities that result from the ignoring of such a common-sense principle.

G. M. B.

PHARMACEUTICAL PESSIMISM.

In a recent letter to the editor, a valued correspondent wrote: "A friend of mine, who is in the advertising business, states that in reading the literature of pharmacy it is very pessimistic and so far he has been unable to obtain an optimistic view. This is quite the contrary to some of the writings he has read in regard to medicine, which have a tendency to glorify the profession."

This comment illustrates again "The Evil of Disparagement" to which attention was directed in our editorial column in the April issue. It is based upon the only too evident tendency among many pharmacists and likewise some American Pharmaceutical journals to disparage the work and position of pharmacy. This internal belittling of pharmacy is too often made the foundation for external criticism and the public's slight estimation of the pharmacists.

The fad of speaking disparagingly of pharmacists and their efforts should long ago have run its course in pharmaceutical circles. It cannot be too strongly condemned. The evil that it has already accomplished cannot be estimated, and the quotation above given is but another evidence of the impressions conveyed to those who are outside of pharmacy. It has been disheartening to the writer, at times, to have belittling and prejudicial statements from pharmaceutical publications offered by government officials, legislators and members of other professions as evidencing the true status of pharmacy.

It is unjust to the vocation that we represent, that the scientific attainments and many public services rendered to mankind by many eminent pharmacists in America as well as in other countries should be ignored and that the public should be given an absolute misconception of the part performed by pharmacy in the discharge of its duty to society as one of the branches of professional medicine.

Pharmaceutical journalists should certainly not be ignorant of the history of pharmacists and their contributions to science and public knowledge and welfare. Pharmaceutical journalism, at least, should be alive to the necessity for changing its attitude and for the edification of the public should not fail to present to the world the many services rendered by pharmacists as evidences of the good faith and professional standing of those who are conscientiously devoting their energies along pharmaceutical lines.

G. M. B.

REPORT OF COMMITTEE ON PHARMACOPŒIAS AND FORMULARIES OF THE NEW JERSEY PHARMACEUTICAL ASSOCIATION.

Before the next annual meeting of the New Jersey Pharmaceutical Association, the convention called for the tenth decennial revision of the Pharmacopœia of the United States will most likely have been held in Washington and another committee of revision have been selected. Hence before this meeting adjourns accredited delegates to represent our State Association at that convention should be selected and their alternates named.

As the plans already adopted provide for the simultaneous revision of the National Formulary so that the fifth edition of that work shall be issued at about the same time as the U. S. P. X and both to become authoritative at the same date, it is, likewise, probable that the committee of revision of the Formulary will be appointed by the American Pharmaceutical Association before our meeting in 1920. Hence it is important that any recommendations relating to these revisions or any instructions to your delegates should be decided upon now.

The plan proposed by Dr. Lyman Spalding for the preparation of a "National Pharmacopœia" with but very little changes therein, has withstood the test of a century. It is truly American and democratic, and as we believe that it secures the most representative gathering of the interests that are concerned in the production of an authoritative materia medica that shall provide for the important needs of the entire country in this respect and supplies the very best talent that is needed for the selection of the Revision Committee, we recommend that this Association endorse a continuation of this plan for the revision of the U. S. P.

It is noteworthy that while the U. S. P. IX has now been before the public for three years, the criticisms and suggestions for improvements and the actual errors pointed out, have been very much less than occurred within the same period after the revisions of 1880, 1890 and 1900. Like all other works of human beings, it has its faults and corrections as well as the changes that have occurred in the medical practices and in the materia medica since 1910, call for the usual decennial revision.

It is believed that the Committee of Revision and the Pharmacopœial Convention will welcome constructive criticisms and suggestions. At the previous convention, your delegates presented in book form a typewritten abstract of all recommendations relating to the Pharmacopœia that had been printed in the proceedings of the New Jersey Pharmaceutical Association during the decade. This was referred to the Committee of Revision and no doubt was of some service in their work. We would recommend that the delegates selected to attend the 1920 convention be instructed to prepare and submit a similar report embodying abstracts from our proceedings and the suggestions and recommendations approved at this meeting.

Your committee are of the opinion that this Association, as well as other pharmaceutical, medical and chemical societies, should enunciate its views upon the general principles that should be followed in the coming revision and likewise upon special topics. With that end in view, we submit the following specific recommendations.

We recommend that the "Scope of the Pharmacopœia" as defined in the U. S. P. IX be retained for the next revision.

We recommend that the admission of an article or preparation to the pharmacopœia be based upon its determined general medical use justifying an official standard. That the dismissal of any article now standardized as a medicament in the U. S. P. IX be based upon a determination that its general use as a medicine is not sufficient to justify its retention.

It is believed that the monographic presentation of standards for the drugs, chemicals and preparations in alphabetical sequence as followed in the preceding revision is the best that can be devised both for reference and clarity of presentation of the subjects and it is recommended that this be continued.

It is especially recommended that the style adopted for titles, synonyms, definitions and "purity rubric" in the ninth revision be

followed in the tenth and that limits of purity in each case be given careful consideration and made as elastic as is consistent with the maintenance of standards of quality and the prevention of fraud and carelessness.

With the changes that are continuously taking place in the source of and markets for pure drugs and also the numerous undertakings throughout the world of the cultivation of drug plants, it is urged that unless absolutely necessary in order to determine quality, the Pharmacopœia omit geographical designations and further that such changes as are due to cultivation, difference in climates or modes of collection and preparation of such drugs be given due consideration in the framing of the standards and tests.

While approving of the principle of the unification of formulas for potent remedies by international agreements, it is our opinion that the conclusions arrived at by the "Conférence Internationale pour l'Unification de la Formulo des Médiçaments Héroiques" held in Brussels in 1902 were not entirely free from faults and that these are not such as would be approved in their entirety at this time. It is recommended that the United States Pharmacopœial Convention should take the initiative in inviting another international conference for this purpose in the near future, preferably, in the United States and that the conclusions be incorporated in the U. S. P. X.

It is believed that the method of stating the chemical formulas adopted in the ninth revision is well suited for the purposes of the pharmacopœia and so it is recommended that the same methods or with only minor modifications, be retained. Also that the atomic and molecular weights employed be the latest available Report of the International Committee on Atomic Weights.

It is recommended that the weights and measures adopted be restricted exclusively to the metric system. In order that the professional interests may be encouraged and likewise that the commerce of the nation may be stimulated it is uregd that the Pharmacopœial Convention give the force of its endorseemnt toward making the use of the metric system universal in medical practices and in the commercial transactions in the United States after a fixed date.

In the eighth and ninth revisions 25° C. was adopted as the standard temperature. The Bureau of Standards of the United States has persisted in maintaining 20° C. and several of the other departments of the federal government prefer to follow the Bureau in this matter. It is obvious that two standard temperatures should

not exist in this country and we have come to the conclusion that 20° C. more nearly represents the normal room temperature in the various sections of the United States and we recommend that in the future revisions 20° C. be adopted for the standard temperature except where in a few determinations, such as those of refractive indices, another temperature may be necessary and that in each such group of necessary variation the temperature to be adopted shall be stated if it varies from the standard.

In order to economize the space and the cost of publication, the U. S. P. IX introduced a plan for general formulas which was tested out in the type formulas given for fluid extracts and for tinctures. This plan has eliminated much useless repetition and appears to have worked entirely satisfactorily and we recommend its extended use wherever practicable in other classes of official preparations.

The previous pharmacopœial convention "recommended that a range of volume content of absolute alcohol be stated in the Pharmacopœia for each preparation containing alcohol." While the recommendation was not carried out in its entirety a partial table of alcoholic content was published in Part II. The importance of such official statements of the range of alcoholic content permissible in each official preparation is apparent to every pharmacist and would be a guide to those entrusted with the enforcement of the laws against adulteration of drugs. It is therefore recommended that wherever possible the U. S. P. IX should give such information.

The necessity for accuracy in the preparation of medicines and in their administration needs no argument. It is recommended that the U. S. P. define and describe standard graduate measures and a standard dosage measure.

The enormously increased use of "biologic products" such as serums and bacterins in medical practice must be recognized. The same is also true regarding the use of many animal organ drugs such as mammary substance, ovarian substance, corpus luteum. It is recommended that especial consideration be given to the necessity for official standards for these.

The Federal Food and Drugs Act fails to recognize any standard for homeopathic drugs and so far the homeopaths have failed in their endeavors to have Congress recognize as a legal authority the Homeopathic Pharmacopœia of the United States and as the coequal of the U. S. P. and N. F. The reason for thus failing to recognize

an authoritative legal standard for homeopathic remedies which are necessarily prepared by different methods from those of the present U. S. P. or N. F. need not be discussed in this report. It is well known that in some sections of the United States, homeopathic drugs have a large use and are sold by many druggists, and legal standards for such that are commonly sold and used should be established and designated by the law. We are of the opinion that the need for standards for homeopathic medicines can at least be met in part by a unification of the pharmacopœial standards. In the ninth revision of the U. S. P. certain innovations were introduced such as the chapters on "Biologic Assays," "Sterilization," and "Diagnostical Reagents and Clinical Tests." It would appear as no greater innovation for the tenth revision to have chapters such as appear in homeopathic pharmacopœias on "Cleansing of Utensils," "Vehicles," "Selection of Medicinal Substances," "Preparation of Potencies and Dilutions." The various classes of preparations used especially in homeopathic practice, such as mother tinctures or fresh drug tinctures, solutions, triturations, etc., could very likely be treated by general formulas. Representation of the Homeopathic Societies in the Convention and a Subcommittee on Homeopathic Standards of the Revision Committee, would readily provide for this part of the revision.

Regarding the revision of the National Formulary, we are of the opinion that the time is ripe for the coöperation of a committee of active medical practitioners in the edition to be soon undertaken. Such a coöperation of the medical societies should be solicited by the American Pharmaceutical Association which owns and controls this publication and should be given by the formation of a committee composed of practicing physicians acquainted with medical customs and usages. In close coöperation with a committee of revision composed of those whose experience and ability as pharmacists should be exceptional, medical assistance would be of great value in simplifying combinations and eliminating a number of the unnecessary and duplicating formulas. Moreover, it should stimulate the acquaintance of the physicians with the various useful preparations in the book and their increased prescribing of these to the advantage alike of the patient and the professions of medicine and pharmacy.

Despite the efforts of the various propaganda to popularize the Pharmacopœia and the National Formulary, it remains still a fact that comparatively few of the physicians are to-day sufficiently ac-

quainted with the formulas of either. Undoubtedly, this is very largely due to the fact that the physician is not as a rule interested in the mass of matter relating to standards and tests that is necessarily contained in these publications. An official epitome of each of these legal standard authorities should be prepared by a joint committee of physicians and pharmacists and these be widely distributed as mediums of education. Such epitomes should present in a readable way the information relating to composition, doses, practical uses and combinations that appeal to the busy practitioner. It must not be made a commentary or an unwieldy dissertation. It is believed that without surrendering in the least the dignity of authority or of position such epitomes of the U. S. P. and of the N. F. can be prepared and would go a long way toward overcoming the indifference of the medical practitioners and too often evident lack of acquaintance with the official materia medica.

THE ANATOMY OF UMBELLIFEROUS FRUITS.[1]

In a series of articles published in the *Schweizerische Apotheker-Zeitung,* Vol. 57, No. 13, pp. 183–188, Joseph Styger describes the macromorphology and micromorphology of a number of umbelliferous fruits. In the first of these articles the author discusses the structure of *Œnanthe Phellandrium* Lam., *O. Lachenalii* Gmel., *O. pimpinelloidea, Æthusa Cynapium* L. and *Levisticum officinale* Koch. as well as the distribution of the first and last named plants. The salient features of these articles are hereby presented:

Œnanthe Phellandrium Lam. The home of this species, commonly known as "Water Fennel," is Europe and Central Asia. The fruits are glabrous, up to 5 Mm. long, 2 Mm. broad and 1.5 Mm. deep, roundish-cylindrical, slightly laterally compressed, yellowish-brown, somewhat acuminate toward the style, crowned with the stylar cushion and sometimes with the bent style. Ribs broad, slightly projecting, the grooves being small and darker than those whose fruits are not so readily split. Under a hand lens the schizocarp is compressed dorsally, the fruit wall being very broad. The broad ribs are slightly projecting, the marginal ribs are strongly built; dorsal surface 1-striped, commissural surface 2-striped. The

[1] Abstract prepared by Prof. Heber W. Youngken.

endosperm is rounded dorsally, somewhat pressed in by the vittæ, on the inner side almost straight; sclerenchyma fibers run at the base of the ribs.

Under the microscope, the upper surface shows tangentially stretched cells with a slightly thickened cuticle. Beneath the epidermis of older fruits lies a parenchyma zone which is collapsed or compressed toward the inner part. The middle portion of the mesocarp is divided into two distinctly demarkated zones. The outer is composed of large, rounded, punctated, thick-walled parenchyma cells which take the red color with phloroglucin and hydrochloric acid, only over the vittæ lies a zone of unthickened collapsed tissue; on the commissural side, the punctuated tissue is small and round celled. The inner part is filled up with strongly lignified sclerenchyma fibers which are especially broad in the ribs (up to six rows of cells thick) and are extended in an almost interrupted row around the oil tubes. A similar patch, also, lines in the region of the raphe, but is not prolonged over the secretory passages. Only the marginal rib-plates stretch over almost half of the vittæ. The bast fibers are long-pointed, with small elliptical pores sloping to the left. The pitted trachea lie on the boundary between the sclerenchyma plates and the thickened parenchyma and are accompanied by thick-walled wood parenchyma. The secretory passages are roundish-oval, up to 110 μ in lengthwise view and 60 μ in transverse view; on the commissural surface they are for the greater part larger (up to 180 μ in longitudinal section and 90 μ in cross section). They border on the inner epidermis and are surrounded by well built, quadrate or weakly peripherally stretched epithelial cells. The seed coat is greatly collapsed, brown-walled, underdeveloped on the commissural surface. The thin-walled endosperm contains fixed oil and aleurone. Other *Œnanthe* species resemble this one and are differentiated in anatomical structures by the arrangement of the sclerenchyma elements and the wood parenchyma.

Œnanthe Lachenalii Gmel.—The thickened wood parenchyma is found only in the ribs, not in the inter-rib regions. The sclerenchyma fibers are arranged as in *O. Phellandrium.*

Œnanthe pimpinelloidea.—As in *O. Phellandrium* the sclerenchyma plates are more broadly developed in the ribs, but are extended over the vittæ in a more layered band, up to four rows broad.

Æthusa Cynapium L.—The fruit of "Fools Parsley" is oval, 4 Mm. long, 2.5 Mm. deep and 2 Mm. broad, pale yellow, crowned

with the stylar cushion and both styles, very slightly cleft. The ribs are somewhat broad, the grooves strongly crowded together. These are pervaded through their entire length by dark-brown oil passages, which are especialy prominent in the dorsal region and extend in arcuate fashion.

As examined with a hand lens, cross sections show the fruit wall to be oval, only nearly straight on the partition surface. The ribs are broad and very strongly projected; both the marginal costal are, moreover, slightly winged. In the middle of the inter-rib regions is an oil reservoir with reddish-brown contents; on the commissural surface are two such secretory passages. The endosperm is rounded dorsally and slightly concave in the region of the raphe.

Under the microscope, the outer epidermal cells are slightly tangentially elongated, over the ribs quadratic. Especially here the outer membrane shows small warts, owing to the parallel cuticular striæ as observed in surface section. The endocarp shows tangentially elongated cells. The inner layer of the mesocarp (60 μ broad and up to 15 cell rows thick) is built of tangentially elongated, strongly compressed cells. The outermost are finely reticulately thickened and surround the fruit like a closed band. The outer broader zone of the middle region is filled up with loose, very thin walled parenchyma tissue. The broad ribs are almost completely filled up with finely reticulately thickened tissue which exhibits a rounded form; its cells are almost regularly polygonal, only those lying along the margin being peripherally elongated. At the site adjacent to the rib ends lies the vascular bundle with a few narrow spiral tracheæ which are only distinctly noticeable in longitudinal section. They are accompanied by narrow-lumened, obliquely punctated and long taper-ended bast fibers. All the thickened elements are lignified. Outside of the fibrovascular strand in each rib lies a small secondary oil reservoir and at times there is found another similar one alongside of the thickened tissue. In the middle of the inter-rib region, bounding the inner thickened mesocarp zone lies a rounded oval secretory channel with reddish-brown contents and from 110 μ long to 75 μ broad. Both of the vittæ in the commissural region are somewhat larger. The seed coat is brown-walled and strongly collapsed; only in the raphe portion is it somewhat broader developed and shows a bending in of the endosperm. The endosperm is uniformly thickened, contains fixed oil, aleurone and rosettes of calcium oxalate from 2–5 μ in diameter. In the

epidermal cells are contained yellow flakes and crystals, often plume-shaped, which are readily soluble in KOH with a yellow color, but insoluble in chloral, alcohol, water and glycerin.

Levisticum officinale Koch.—The habitat of this species, commonly known as "Lovage," is unknown, apparently Southern Europe; moreover, it is doubtlessly unknown as growing wild. It is cultivated in large quantities in the province of Sachsen, in Thüringen, Holland and France, and considerably in the garden as a cooking aromatic.

The fruits are quite scissile, the schizocarp up to 7 Mm. long, 3.5 Mm. broad and 1.2 Mm. deep, yellow to dark brown, mostly straight, seldom only slightly bent, ovate-oblong, crowned with the broad stylar cushion and at times also with the bent style. The ribs are small and project strongly outward. Under a hand lens, the somewhat dorsally compressed mericarp is stretched, on the commissural surface, almost straight. All the ribs are strongly marked; the border ribs are wing-like, the latero-dorsal ribs are moved toward the midrib, so that both sides of the section appear only very slightly concave. There is a vitta in the tissue between each two ribs on the dorsal side. The commissural side shows two vittæ. The endosperm is oval and shows a slight concavity on either side of the raphe.

Under the microscope, the outer margin of the fruit is composed of proportionately large, quadratic or, in part, of somewhat higher than broad epidermal cells whose outer membrane is very finely warty. The endocarp cells are small and elongated. The whole mesocarp is composed of thin-walled, hollow and large-celled parenchyma. The fibrovascular bundles occupy the middle region of the ribs and are especially thickened toward the outer and inner epidermis. The few spiral tracheæ are accompanied by long-pointed, narrow-lumened and obliquely punctated bast fibers. Bordering the inner epidermis lie the secretion reservoirs (vittæ) of elongated oval form, 135 μ long and 30 μ broad. The commissural vittæ are generally somewhat smaller. The dorsal vittæ can attain a length of 195 μ. The outer part of the testa is alone well kept and show slightly tangentially elongated right-angled cells. The inner seed coat is collapsed. The nourishing tissue is uniformly slightly thickened and contains fixed oil and aleurone.

RELATIVE SENSITIVENESS OF THE FEHLING, PHENYL-HYDRAZINE AND NYLANDER TESTS FOR THE DETECTION OF DEXTROSE IN URINE.

By George E. Ewe,

PHILADELPHIA, PA.

Standard Material Employed in Tests.—Merck's chemically pure dextrose rendered anhydrous at 40° C., dissolved in proper proportion in distilled water to make standard solutions of the various strengths employed in the tests. Since the experiments extended over several days fresh solutions were prepared each day.

Nylander's Test.—Formula: Rochelle salt 4 Gms. dissolved in 100 Cc. of 10 per cent. sodium hydroxide solution, warm and add 2 Gms. bismuth subnitrate.

Application of Nylander's Test.—One volume of reagent was added to 10 volumes of dextrose solution; the mixture then being heated for 5 minutes in boiling water. A black coloration was taken to indicate dextrose.

Fehling's Test.—Formula:

Copper sulphate (cryst.)	34.639	Gms.
Sod. hydroxide sol. (sp. gr. 1.120)	500	Cc.
Rochelle salt	173	Gms.
Water qs.	1000	Cc.

Dissolve copper sulphate in 100 Cc. warm water and dissolve the Rochelle salt in the sodium hydroxide solution. Mix these 2 solutions slowly and add enough distilled water to make a yield of 1,000 Cc.

Application of Fehling's Test.—The Fehling's solution was placed into a test tube up to about 1 inch from the bottom of the tube; the solution was brought to a boil and a few drops of the dextrose solution was added. The mixture was then boiled for a minute. If no apparent reduction was observed the dextrose was added in sufficient quantity to obtain a reaction but not in greater volume than the volume of Fehling solution employed in the test. In applying the test to the dextrose solutions having a percentage of 0.0625 per cent. or less equal volumes of the Fehling solution and

dextrose solution were employed, boiled for one minute and set aside for one half hour to allow any precipitate to settle.

In all the tests blanks were run on the Fehling solution using distilled water in place of the dextrose solutions.

Phenyl-Hydrazine Test.—Formula: A mixture of 1 Gm. Phenyl-hydrazine hydrochloride, 2 Gms. sodium acetate, and 10 Cc. water was shaken together and 2 drops of glacial acetic acid was added. The solution was again shaken well and then filtered clear. This reagent was prepared fresh daily in these experiments.

Application of Phenyl-Hydrazine Test.—Five Cc. of the reagent was added to 10 Cc. of the dextrose solution in a test tube. The tube was placed in a beaker of boiling water and the water was boiled for one hour. The tube was then removed from the boiling water and allowed to stand at room-temperature. The appearance of the characteristic crystals of phenyl-glucosazone in the test was taken as a positive reaction. In solutions of dextrose of 0.125 per cent. strength and above, the crystals were formed in the hot liquid in less than an hour from the beginning of the application of the heat. In solutions of 0.0625 per cent. and less, the crystals formed after boiling for one hour and allowing to cool for various periods of time.

Keeping Qualities of Phenyl-Hydrazine Test Solution for the Detection of Dextrose in Urine.—Phenyl-hydrazine test solution is not a perfectly stable solution, but possesses much greater stability than it is usually credited with. The following experiments tend to prove this:

A quantity of the test solution was prepared as mentioned above and placed in an amber-glass bottle equipped with a ground-glass stopper. This supply of solution was kept at room temperature for 19 days and tested for sensitiveness at various times during that period. The results of these tests follow:

Strength of Dextrose Solution	Age of Test Solution	Reaction
0.005 per cent.	Fresh.	Positive after cooling and standing 45 min.
0.005 per cent.	2 days.	Positive after cooling and standing 55 min.
0.005 per cent.	6 days.	Positive after cooling and standing 75 min.
0.005 per cent.	10 days.	Positive after cooling and standing 90 min.
0.005 per cent.	19 days.	Negative after cooling and standing 24 hrs.

The comparative sensitiveness of the three tests for the detection of dextrose in urine are shown in the following table:

Strength of Dextrose Sol. (Percentage).	Phenyl-Hydrazine Test.	Fehling's Test.	Nylander's Test.
0.5	Positive before cooling.	Positive while hot.	Positive (black coloration).
0.25	" " "	" " "	Positive (brown coloration).
0.125 ...	" " "	" " "	Positive (light brown coloration).
0.0625 ..	" after "	" " "	Positive (very light brownish).
0.06	" " "	" " "	Negative.
0.03125 .	" " "	" " "	
0.0156 ..	" " "	" after standing.	
0.01	" " "	" " "	
0.009 ...	" " "	" " "	
0.008 ...	" " "	" " "	
0.007 ...	" " "	.....	
0.006 ...	" " "	.....	
0.005 ...	Positive after cooling. and standing for 45 minutes.	Positive after standing.	
0.004 ...	Positive after cooling and standing for 1 hour.	.....	
0.003 ...	Positive after cooling and standing 1 hour 20 minutes.	.....	
0.0025 ..	Positive after cooling and standing for 1¾ hours.	Positive after standing.	
0.002 ...	Negative (amorphous deposit) after standing for four hours.	.....	
0.00125 .		Positive after standing	
0.000625		Negative after standing for ½ hour.	

Conclusions.—Nylander's Test is not of much value for the testing of solutions containing less than 0.5 per cent. dextrose.

Fehling's solution is the most sensitive, showing positive reaction with a solution containing only 0.00125 per cent. of dextrose.

The phenyl-hydrazine test is highly sensitive, showing positive reaction with 0.0025 per cent. dextrose solution after allowing the test to cool and stand for 1¾ hours.

Phenyl-hydrazine test solution possesses fairly stable keeping qualities.

The above experiments and conclusions were made in the Spring of 1907, at the suggestion of Prof. G. H. Meeker, then professor of chemistry of the Medico-Chirurgical College, Philadelphia. Pa. In 1908, Meeker and Stamm[1] independently duplicated these exper-

[1] *Bulletin of the Medico-Chirurgical College of Philadelphia,* Dept. of Pharmacy, Vol. III, No. 3, Feb.–March, 1908, page 15.

iments and arrived at essentially the same general conclusions. The experiments and conclusions outlined in this paper are herewith offered merely as additional evidence upon the subject of the relative sensitiveness of these tests.

A STANDARDIZATION OF DIGITALIS PREPARATIONS.[1]

By Edgar Berry, M.Sc., A.I.C.

In presenting the following treatise I wish to thank H. E. Annett, Esq., M.D., D.P.H. (late professor of comparative pathology of Liverpool University), who has very kindly performed the injections for the Minimum Lethal Dose experiments, I myself not being licensed for this, and also Messrs. Evans Sons, Lescher and Webb, Ltd., for permission to publish results obtained in their research laboratories at Runcorn.

From my last investigation of Digitalis Purpurea (*P. J.*, Dec. 26, 1915), based on frog heart perfusions, three conclusions were drawn.

1. The water-soluble glucosides of digitalis apparently have the most desirable tonic and slowing effect on the heart, and are non-cumulative and non-toxic.

2. Digitoxin is cumulative and toxic, appearing to enter into actual combination with the heart muscle.

3. The leaf saponins have a harmful and toxic effect on the heart.

The constituents of digitalis vary to a very large extent under different conditions of growth. This variation is influenced by climate, soil, conditions of growth (sunshine or shade), humidity, and period of growth. For example, I found a sample of Spanish leaves to be very rich in saponin, although, apart from this, the perfusion experiments showed a good physiological action. Again, a tincture made from the first large leaves of seedlings of four months' growth from the first appearance of leaves, packed closely together in cold frames (thus excluding sunlight), I found to have the action of pure water soluble glucosides, digitoxin apparently not yet having been formed.

From these considerations—in view of the number of existing official preparations containing the whole of the soluble constituents

[1] Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 26, 1919.

of digitalis—it is of great importance that attention should be drawn to their standardization.

Many methods have been put forward within the last few years, but none are entirely satisfactory when taken alone.

The favorite method of standardization has been by the Minimum Lethal Dose method—that is, the amount (calculated per 100 Gms. body weight) which, injected into the lymph sac of the frog, is just sufficient to kill.

Different physiologists place different time limits on this experiment—some two hours, four hours, six hours, etc. A few hours after injection the frogs become very lethargic, and it is extremely difficult to differentiate with any degree of accuracy between slight reflexes and total death. In several cases I have known frogs from which no reflex could be obtained at the end of the fourth hour, recover during the night.

Again the strength of tinctures containing excess of saponin comes out too high by this method—notably the tincture from Spanish leaves which I mentioned before—although when the drug is taken by the mouth the action is weak, digitonin (saponin) being unabsorbed in the intestine.

A sample containing a high percentage of water soluble glucosides was under strength when tested by this method, although on perfusion its action was quite powerful and desirable.

The objections to the Minimum Lethal Dose method (by injection) are:

1. A large number of frogs is required for each sample.

2. A vivisection license is necessary, and consequently the chemist cannot standardize his samples by this means.

Up to the present the best standardization put forward for digitalis preparations is Dr. Martindale's colorimetric estimation.

This method gives very concordant results with the M.L.D. values and eliminates frog variation; but, unfortunately, it does not differentiate between saponin and digitalein, and, furthermore, does not give the full digitoxin strength, some of the latter being undoubtedly precipitated along with colloidal matter on the dilution of the original tincture with water (the alcohol strength not being sufficient to hold it in solution) or is "absorbed" by the kieselghur used in filtration. As the digitoxin content does not run parallel with the digitalein in all samples (which I mentioned before), this

may give rise to inaccurate results, especially when dealing with tinctures of which the history and origin are unknown.

Some investigators claim to have standardized digitalis preparations by the use of "pithed" frogs and the Williams Apparatus, injecting the drug and noting (1) the time taken to kill the heart, and (2) the number of heart beats; calculating their results from standard tinctures of digitalis or from solutions of strophanthin. From my own tests I have not found this method reliable.

M.L.D. methods by injection show toxicity only and not therapeutic value.

Perfusion Experiments.

The apparatus used was in some respects similar to that described in my first paper (*P. J.*, Dec., 1915). I found it necessary to modify it very considerably.

The glass reservoir A contains Ringer's normal saline solution. B contains a solution of the tincture to be tested 1 per cent. in Ringer's solution.

The reservoirs were fitted with internal tubes as before (to keep the pressure constant). The stand which carried these was graduated on the upright, the zero mark being placed in such a position that the level of the lower ends of the air-tubes A and B were the same height from the table as the end of the canula C. The pressure is thus regulated by raising or lowering the cross-arm S. The Y tube, mentioned before, was substituted by a combination of three 3-way taps, which I found much more convenient than clips. The frog was "pithed" and dissected as before, a glass canula being inserted into the inferior vena cava and carefully ligatured, care being taken that no leakage was possible at the joint—the two aortæ were left intact in this experiment and the solutions perfused through the body to the other cut end of the inferior vena cava, which was left open, thus allowing the perfused solutions to escape from the body, through the perforated frog plate, into the tray T, and thence to the outlet "N," which is a glass tube of ⅛ in. bore. The drops of liquid from here operate the small trigger "K," which was counterbalanced and connected up with the writing lever "R"; thus each drop was registered on the tracing.

"S," the heart lever, is connected to the heart as before.

"F," the time marker, registers every five seconds.

The apparatus was arranged so that the height of the air-tubes

was 2 Cms. above the level of the canula "C," the solution thus being delivered at a slight pressure. The technique of the perfusion may be found on referring to my first paper. Previous to the experiment the saline content of the glass canula and tube as far as the tap "X" was accurately measured in drops for each canula, and this amount allowed for in the tracings.

It seemed feasible if the same conditions were maintained as regards (*a*) rate of flow of the perfusing solutions—*i.e.*, constancy of pressure from the supply reservoir—and (*b*) the use of solutions of equal percentage strength, that the quantity of liquid perfused through the heart should be directly proportional to the strength of the preparations used.

In this perfusion test only a certain proportion of the active constituents are used up; but we may reasonably assume that, provided the above conditions are observed, the amount absorbed by the tissues will be proportional to the weight of the hearts used; or, carrying this hypothesis still further, to the respective body weights of the frogs used (subject, of course, to slight frog variation). The amounts used, therefore, reduced to the values per 100 Gm. frog, should be directly proportional to the strengths of the solutions, and thus to the respective M.L.D.'s.

The following table of results, calculated per 100 Gm. frog weight, was obtained from various tinctures by this method. The M.L.D. of each tincture was obtained by the colorimetric estimation, and also by the actual Minimum Lethal Dose method by injection, and recorded in the table.

The time taken to kill the heart in these experiments showed no striking similarities. This discrepancy is probably due to the variation in relative quantities of the several glucosides present.

Summarizing the table, the quantity of solution necessary to kill the heart (recorded on the tracing in drops) approximates very nearly in tinctures of the same Minimum Lethal Dose, and is directly proportional in tinctures of different strengths. The values obtained, I admit, are merely measures of toxicity, but the therapeutic action can be actually seen during the experiment, and excess of any one glucoside may be easily detected in the tracing. Although these results approximate fairly well, yet I do not consider them sufficient for the standardization of a tincture by this means alone.

Considering the subject now from a chemical standpoint, the solution of the difficulty seems to lie in estimating the relative quan-

Preparation Tested.	Expt.	Number of Drops Perfused Calculated per 100 Gm. Frog.	M.L.D. from Graph.	M.L.D. Colorimetric.	M.L.D. by Injection.
Tinct. B.	1	1032	0.605	0.6	0.55 0.6
"	2	1032			
"	3	1031			
Tinct. 10	1	649	0.5 to 0.55	0.75 much deposited since perfusion expt. was done.	No data
"	2	579			
Standard Tinct. 2...	1	1063	0.615	0.65	0.6 to 0.65
" "	2	1064			
Tinct. 21.3.18	1	640	0.43 to 0.48	0.4 to 0.5	0.4
" "	2	540			
Tr. from Extract Dilution 1 in 10	1	1008	0.6	No data	0.6
Dilution 1 in 7.5....	2	726	0.51.	No data	0.45
Tinct. 5	—	561	0.45	0.45 to 0.5	No data
Tinct. A.	—	517	0.43	0.4 to 0.45	No data
Standard Tinct. 1, 29.9.16	—	1231	0.67	0.6 to 0.75	0.7

tities of the glucosides present. I therefore devised the following colorimetric processes.

These are partly on the lines of Dr. Martindale's method, but essential differences will be found in the extraction, precipitation, filtration, and also in the "working up" of the resulting glucosidal residues.

Colorimetric Process A: For Water Soluble Glucosides.

In this estimation the idea is to obtain the water soluble glucosidal content only, and to eliminate digitoxin and saponin. Alcohol is removed from the tincture to be tested and cold water solutions are used to eliminate as much digitoxin as possible, this glucoside being almost insoluble in cold water. Extraneous matter is removed by treatment with lead acetate solution, filtration being effected through kieselguhr plates in Buchner funnels. Excess of lead is removed by sodium phosphate, and the solution again filtered through kieselguhr. Precisely the same conditions must be observed in each estimation, and similar amounts of kieselguhr used.

In this way any traces of digitoxin are also eliminated by "adsorption." The solution is now evaporated on the water bath in the presence of chalk, and the residue purified by solution in methyl alcohol and chloroform and filtration. Saponin is then precipitated by the addition of ether, filtered off, and the filtrate evaporated to dryness. At the various stages aliquot parts of the solution are taken to avoid loss in filtration, and the experiment arranged so that the final residue is equivalent to 7.5 Cc. of the original tincture. The final residue is dissolved up in 3 Cc. of glacial acetic acid. .2 Cc. of this solution is then mixed with 2 Cc. of Frohde's reagent in a 4 in. × ½ in. test tube, allowed to stand for fifteen minutes, and the color produced compared with the color chart.

(= Values for experiment A.)

The color chart is painted from actual estimations, and requires a little explanation.

The "Equivalent Minimum Lethal Dose" values are noted separately under each color for each of the two colorimetric estimations.

The "relative strength" values denote the amount of glucosides extracted in the various colorimetric estimations, taking the color produced by the water soluble glucosides extracted from a standard tincture (M.L.D. by injection = 0.75) by process A, as unity.

Process B: Colorimetric for Total Glucosides.

In this second estimation an alcoholic strength of 70 per cent. is maintained throughout, in order to keep all the glucosides in solution. The extraneous matter is removed by lead acetate, but is filtered off through ordinary filter paper only, *no kieselguhr* being used. The excess lead is removed by sodium phosphate, and the filtrate evaporated to dryness in the presence of chalk to prevent hydrolysis. The glucosides are dissolved out by repeated extraction with chloroform, the solutions being filtered, bulked, and evaporated to dryness. Aliquot parts of the solution are taken at the various stages as before, to avoid loss in filtration, and the experiment is arranged so that the final residue is equivalent to 7.5 Cc. of original tincture. The final residue is dissolved up in 3 Cc. glacial acetic acid. 0.2 Cc. of this solution is taken and mixed with 2 Cc. of Frohde's reagent in a 4 in. × ½ in. test tube as before, and, after

standing fifteen minutes, is compared with the color chart, noting the values for experiment B.

The colors produced in this process (B) are much darker than in process A. They are also more inclined to approach a reddish-brown shade. This is due to the presence of *all* the glucosides in the residue, and probably impurities, such as traces of chlorophyll.

This, however, is immaterial, as it is the "*density*" of the color which we must compare.

The correct way to match the colors is to examine the tubes by direct transmitted light, with the eyes wide open, holding a piece of white paper behind them at an angle of 45°. Then slightly close the eyes and look at the color chart.

In process B, should the value compare with tubes "d" or "e," it is too dense to be judged with accuracy on the first color chart.

A more dilute mixture must be made. This is accomplished by taking 0.1 Cc. only of the acetic glucosidal solution and introducing it into 4 Cc. of Frohde's reagent, allowing to stand for fifteen minutes, and then comparing the tubes with the second chart.

The value may thus be accurately determined, as the "relative strength" values on Chart 2 are strictly comparable with those on Chart 1, the colors having been painted directly from known tubes and the "relative strength" values worked out and checked by experiment.

The result from Process A gives *water soluble glucosides only.* This I shall call the "Therapeutic Value" of the tincture.

The result from B gives *Total Glucosides*—viz., water soluble glucosides, saponin and digitoxin. (The residue here is not very pure, but this does not greatly affect the colorimetric estimation, whereas weighing would be inaccurate.) Subtracting A from B we get the "Toxic Value" of the tincture.

We can therefore compare toxicity by means of the ratio

$$\frac{B-A}{A} \textit{ i.e., } \frac{\text{Toxic Value}}{\text{Therapeutic Value.}}$$

If we estimate this for a standard tincture and for an unknown tincture, and compare the two (using "relative strength" values) we can compare the toxicity of the samples, as in the following example:—

	Standard Tincture.	Tincture 213.18.
Therapeutic value (A) ... (W. S. Glucosides)	1	1.5
Total Glucosides ..... Value B	2.5	4.0
Toxic Value (B–A)	1.5	2.5
Ratio $\frac{B-A}{A}$ =	$\frac{1.5}{1} = 1.5$	$= \frac{2.5}{1.5} = 1.66$

thus showing that the Tincture (213.18) is relatively more toxic and therefore not so beneficial as the Standard Tincture.

A desirable standardization of any tincture would be as follows: (1) Conduct two colorimetric estimations by process A and B. Note the M.L.D. value, and the therapeutic value (A). Then check the M.L.D. value from experiment B, and work out the ratio $\frac{B-A}{A}$. An increased M.L.D. value from (B) denotes excess toxicity, which would be confirmed by the ratio $\frac{B-A}{A}$. The excess toxicity may be due to either saponin or digitoxin (although for oral medication the presence of saponin is of little import, as I mentioned earlier).

(2) Carry out the perfusion experiment, using male frogs and the tincture 1 per cent. in Ringer's solution, continuing the perfusion until the heart stops. Then calculate the number of drops required for 100 Gm. frog, and find the result on the M.L.D. graph. Notice the time taken to kill the heart, as this gives some guide as to the relative quantities of the several glucosides present—*e.g.*, a long tracing with, say, 0.5 to 0.6 M.L.D. would indicate a high water soluble glucosidal value and a corresponding low digitoxin value and *vice versa*. The tracing would also show the therapeutic action; any abnormal variation in the composition of the tincture being easily detected. (This was explained at length in the treatise which I summarized previously.)

A second "two or three minutes" perfusion on another frog, reperfusing Ringer's solution again to recovery, would give us useful information as regards therapeutic activity. The M.L.D. values obtained from the graph could be checked by injection if desired by using four frogs only, the doses given being

(1) Slightly *below* the calculated M.L.D.
(2) and (3) M.L.D. *as calculated.*
(4) Slightly *above* the calculated M.L.D.

No. 1 frog should live. Nos. 2 and 3 frogs should be questionable. No. 4 frog should die.

I do not consider these injection experiments necessary, and consequently no license would be required for carrying out the standardization.

From the foregoing experiments it is now easy to judge whether a tincture is desirable or not, and to estimate accurately its strength. After adjusting the tincture it should be rechecked.

In conclusion, too much stress cannot be laid on the methods of cultivation of the drug. The best strains of plants (tested by experiment) should be used, and the gathering of the leaves done under strict supervision. These items should be carried out year by year under as nearly the same conditions as possible, if uniform tinctures are to be obtained.

IODINE TINCTURES, WATER SOLUBLE.[1]

By Torald Sollman, M.D.,

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Proprietary preparations of iodine have been on the market for many years and advertised to physicians as superior to the official preparations—tincture of iodine and Lugol's solution (Liquor Iodi Comp., U. S. P.). The superiority claimed for these proprietary preparations is based on the allegation that the potassium iodide in the official preparations causes a local irritant action which is avoided in the proprietary preparations. The allegations seem improbable—certainly the local irritant action of potassium iodide must be regarded as negligible, as compared with that of hydriodic acid contained in the proprietary preparations. Rather, it was surmised that any difference in local irritation following the use of the proprietary preparations was due to the fact that the iodine content in these preparations was insufficient to produce the irritation or, on the other hand, sufficient to have only a slight, if any, therapeutic effect.

[1] From the Department of Pharmacology of the Western Reserve University School of Medicine. Reprinted from the *Jour. Amer. Med. Assoc.*, Sept. 20, 1919. This investigation was supported by a grant from the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association.

The manufacturers do not seem to have published, and presumably do not possess, any comparative data on the degree of irritation produced by their preparations, as compared with the official tincture of iodine after this has been diluted so as to reduce its iodine content to that of the proprietary preparations. It was therefore decided to determine this point by applying various iodine preparations of an equal iodine content to the skin and also by extending the experiments in other directions. In these experiments two widely advertised proprietary preparations—Burnham's Soluble Iodine[2] and Sharpe and Dohme's Surgodine[3]—were included.

Since these, however, are more or less secret in composition, I have devised a non-secret preparation of the same character by the use of hydrogen iodide (hydriodic acid). The details of this preparation will be published in a pharmaceutical journal. Before use, each of these preparations was reduced by the addition of alcohol to a free content of 2.2 per cent. (2.2 Gm. in 100 Cc.).

COMPOSITION OF IODINE PREPARATIONS USED.[4]

Nature of Preparation.	Free Iodine.	Percentage of Combined Iodine (Including HI).	Acidity as of HI.
Alcoholic solution	2.2	0.4	0.2
U. S. P. tincture (KI)	2.2	1.6	0.07
Alcohol with HI (author's formual)	2.2	0.7	0.6
Burnham's Soluble Iodine	2.2	2.7	1.4
Surgodine	2.2	1.2	0.8

The accompanying table shows the composition of the solutions used, the total iodine being the same, the principal difference being in the acidity, which ranges from a minimum of 0.07 per cent. in the U. S. P. tincture (containing potassium iodide) to a maximum

[2] Examination in the A. M. A. Chemical Laboratory indicated Burnham's Soluble Iodine to be a solution of iodine in alcohol made miscible with water by the presence of some iodide and containing approximately 3 Gm. of free iodine and 2 Gm. of combined iodine in approximately 100 Cc. (*J. A. M. A.*, 50: 1055 (March 28), 1908).

[3] The A. M. A. Chemical Laboratory reported that Surgodine was an alcoholic liquid containing 2.51 Gm. of free iodine and 1.78 Gm. of combined iodine, probably present chiefly as hydrogen iodide, in 100 Cc. (*J. A. M. A.*, 70: 257 (Jan. 26) 1918).

[4] The numbers represent grams per hundred Cc. of preparation. Before use, each preparation was reduced with alcohol to a content of 2.2 per cent. of free iodine.

of 1.4 per cent. in Surgodine. The special preparation which I devised is intermediate and contains 0.6 per cent. The total combined iodine (including potassium iodide or hydrogen iodide) ranges from 0.4 per cent. in the alcohol solution to 2.7 per cent. in the Burnham preparation.

Effects on the Skin.—The solutions were painted on the skin of the inner surface of the forearm, each solution covering an area of from 15 to 20 Mm. diameter; each application was allowed to dry before the next was added.

The results did not show any significant or constant differences. The actual results indicated that Burnham's preparation was the more irritant, and the U. S. P. tincture (reduced to the same iodine percentage) was the less irritant, but the differences were so small that they could easily be accidental.

In a preliminary test with three applications, no material difference could be detected between the different solutions.

In a second series, a measured quantity of solution was applied to two spots in three courses. The first course consisted of five applications at intervals of five minutes, and then a pause of thirty-five minutes. At the end of this time, the skin of all the areas was slightly tender. The second course consisted of five applications during sixteen minutes, and then a fifty-five minute interval. There was now considerable tenderness, alike for all the areas. The third course comprised five applications during fifteen minutes. Forty minutes after the last application, all the areas were equally sore. The depth of the stains ran in decreasing order from Burnham's (most) through Surgodine, hydrogen iodide, U. S. P. tincture, and alcoholic (least); but the differences were not great.

After removing the excess of iodine with alcohol, the reddening and edema at this time appeared as follows: Burnham's most, distinct papular edema and reddening; then the alcoholic; then the others, which were about alike.

On the following morning, the order of irritation was as follows: most, both Burnham's areas; next, one of the alcoholic areas; next one of the hydrogen iodide areas; next, Surgodine; least, U. S. P.

Precipitation of Albumin.—Irritation is often due to precipitation of proteins, and this probably applies to the irritant action of iodine. Therefore an investigation was made to determine whether

there exist significant differences in this respect between the several iodine preparations.

Each of the diluted iodine preparations (2.2 per cent. iodine) was diluted with 10 volumes of water, to avoid precipitation of protein by the alcohol, and the diluted solution added to an equal volume of a 10 per cent. solution of natural egg-white in physiologic sodium chloride solution.

The simple tincture, that with hydrogen iodide, Burnham's preparation, and Surgodine, produced an apparently identical coagulum. The U. S. P. tincture (diluted in the same way) produced only a turbidity; this also when the quantity of the iodine solution was doubled. Next morning, the albumin was coagulated as with the others. The reaction to litmus remained neutral.

The restraining action of the potassium iodide is limited, for the addition of an equal quantity of the potassium iodide tincture to the hydriodic acid tincture does not prevent immediate coagulation (1 volume potassium iodide tincture, 1 volume hydrogen iodide tincture, 10 volumes of water).

It is evident, therefore, that the potassium iodide of the official tincture has a restraining effect on the coagulation of protein. This would tend to make it less irritant than the other preparations. It is conceivable that this may be disadvantageous in skin protection, in which the fixative action is probably desirable. In this case, however, there is no object in using a water-miscible preparation, and the simple alcoholic solution of iodine would be fully as good as any of the others.

Capillarity and Spreading.—Dilute tinctures of iodine, when placed on the skin or on parchment, tend to distribute themselves so that the solution becomes most concentrated at the periphery (as in the accompanying illustration). In this manner, the periphery of an application on the skin may be blistered when the center is scarcely affected. If this property were more marked in one specimen than another, this would be equivalent to greater irritation. The illustration shows that this uneven distribution runs in the order: U. S. P. (potassium iodide tincture), most; Burnham's soluble iodine; hydrogen iodide tincture; Surgodine; alcoholic tincture (containing no potassium iodide), least.

The differences are in favor of the simple alcoholic tincture (which was formerly official) and adverse to the tincture containing potassium iodide (which is now official); but they do not im-

press me as of great importance, since they are even less marked on the skin.

I tried also to demonstrate differences in capillarity by the spreading or rise through filter paper; but the variations were insignificant.

Conclusions.—The presence of potassium iodide in the official tincture of iodine does not seem to render this preparation more irritant. On the contrary, it is somewhat less irritant to the skin, and much less precipitant to proteins, than the simple alcoholic tincture, or the secret and non-secret "miscible tinctures." The more even spreading and the more rapid coagulation of protein render the simple alcoholic solution of iodine probably the best for the "disinfection" of the skin; while the delayed protein precipitation by the U. S. P. tincture would probably render this somewhat superior for the disinfection of open wounds. The secret and non-secret "water-soluble tinctures" do not appear to have any material advantages.

PURIFIED ETHER AND THE VARIATIONS IN COMMERCIAL SAMPLES.[1]

By A. J. Jones, Ph.C.

To bring before the notice of the Conference such a subject as ether almost requires apology, for it is one that has received a good deal of attention in the past, and little can remain to be said about it that is really new. But, after making some comparisons between commercial brands, it was thought there were one or two points of interest that would bear consideration, and upon which attention would not be wasted. As everyone knows, there is "ether" and "purified ether"; the former being for the ordinary requirements of medicine and pharmaceutical practice, while the latter is usually taken as having been specially defined for employment as an anesthetic. Purified ether, however, finds other uses, and in some branches of manufacture it is necessary to be very strict in limiting traces of impurities; but it is not so much the object of this paper to enter into that part of the question as it is to draw attention to certain differences existing between what is called by the makers

[1] Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 26, 1919.

"anesthetic ether" and the definition of the "purified ether" of the Pharmacopœia. The results of the examination of nine samples of "Ether Purificatus" prepared by different manufacturers is set out below for illustration. The Pharmacopœia does not demand that ether shall be made according to any particular recipe, but it defines the *character* of the ether, by prescribing a definite specific gravity and a limited boiling point range, and then makes special requirements as to *impurities,* leaving little doubt as to the intention of providing a fairly pure ethyl oxide.

The Character of the Ether.

A glance at the table will show seven samples from industrial methylated spirit, and two from rectified. The latter, as one would expect, are B.P. in character, but of the seven methylated ethers only two answer this description, and the deviations afford interesting comparison. Now it is difficult to believe that, with differences of this sort, identical results are to be obtained from the administration of the different ethers, and since employment as an anesthetic is the use, perhaps, to which importance attaches most of all, this question of uniformity of product and effect is one deserving some consideration.

One is sometimes met by the statements from different surgeons that it is only particular brands of ether that give them satisfactory results, and others again will only use ether prepared from rectified spirit; while a case occurred only a short time ago where an officer connected with an American military hospital, expressed himself as being so dissatisfied with English ether that he gave up using it, and imported all his further supplies for that hospital from America. One is apt to attribute this sort of thing simply to prejudice, but it by no means follows that that is the proper view to take, and I believe it is not very far from the truth to say that during the war a special demand was made for B.P. ether, and that special facilities were given by the authorities for its conditional production. In this connection there is a particularly interesting report by Dr. Cotton of the McGill University, Montreal, on his observations concerning the physiological effects of ether and their causes. His opinions are rather startling, but as they appear to have been demonstrated and to have received certain acceptances they may be briefly stated. Shortly put, he considers that absolutely pure ethylic ether is not

anesthetic in the full sense of the term; that it is narcotic, but not analgesic, and that it is to traces of certain "impurities" formed in the manufacture of the ether to which the proper anesthetic effects are due; suggesting ethylene as being the analgesic substance. In furtherance of this view, some remarkable demonstrations were given of the combined effect of ether and ethylene, but beyond mere mention of this I must refer those interested in the matter to the original communication.[2] The point that it is desired to emphasize in these notes is: Is there any real difference between the action of these low boiling mixed ethers and the higher boiling official article, and is there any valid reason for the preferment of the one to the exclusion of the other from the Pharmacopœia? The difficulty is that one cannot but suppose there were definite reasons for making the restrictions of the Pharmacopœia, yet there remains the indisputable fact that very large quantities of unofficial "anesthetic ether" are requisitioned (even, perhaps, larger quantities of this than of the literally official article) and apparently used with success. If there is no practical difference, then it is very desirable that the official requirements should be modified so as to include both types; but if an undoubted difference is observable, then it is still more desirable that the two types should have recognition, so that all ambiguity might be removed and a distinction drawn as to the special adaptations of the particular ether. This question is one the solution of which is medical rather than pharmaceutical, for it is to do with observed physiological effect; but it is certainly very desirable for the pharmacist to know exactly where he stands when he is called upon to handle material ostensibly the same, but virtually different, which is used without recognition of probable differences in properties.

Closely connected with this is the demand for "absence of methyl compounds" from purified ether. One might, perhaps, be allowed to express the opinion here that it would be a great advantage in cases of this sort where mere traces are being dealt with, if something rather more specific than bare *absence* of a *class* of compounds was required. This is all very well where the desire is simply to maintain a standard of commercial purity, but it is an entirely different thing when tests are introduced having behind them the idea of physiological effect. Such tests should be very distinctly noted and treated in as fully an explanatory a manner as possible. For

[2] *Journ. Canad. Med. Soc.*, Sept., 1917; *Med. Rec.*, Mar. 16, 1918.

purity alone can safely be left to the discretion of the pharmacist whenever discretion becomes necessary, but he is not at liberty to exercise this function in requirements which are specifically medical. Absence of direction of this sort occasionally leads to vexatious proceedings; at times it retards output; at others, through ignorance in giving but secondary consideration to a matter which may really be of primary importance, a very unsatisfactory position of affairs may be brought about.

The Impurities.

The Pharmacopœia prescribes tests to limit the quantity of peroxide, aldehyde, vinyl alcohol, and methyl compounds, and the usual supplies of purified ether behave with general satisfaction in these respects. One or two remarks, however, may be permissible. The test for methyl compounds would be more correctly described as a test for the presence of methyl alcohol and such substances as break down to formaldehyde under the influence of the oxidation. Complaints have been made that the test is erratic in its indication, and it is believed the test was not inserted in the Pharmacopœia with the unanimous approval of manufacturers. Faults of sensitiveness have been mentioned (Dott, *P. J.*, 17/3/17, p. 236) and ascribed both to the fuchsin and to the method of preparing the reagent. Different samples of fuchsin do undoubtedly vary, but I have been fortunate in having samples that never failed to detect so small a quantity as 1 Mgm. of methyl alcohol in 5 Cc. Experience has shown, however, that a Schiff's reagent which may be very sensitive when freshly made is preferably not used after six weeks' keeping; at three months it is useless for the purposes of this test. It has been pointed out (Dott, *C. and D.*, 20/2/15, p. 52) that highly purified methylated ether and ether from rectified spirit will give positive reactions, and this can readily be confirmed. It appears to be due to traces of compounds occurring in the ether, quite apart from its origin, but rectified ethers seem to give a fairly constant indication of about an apparent 0.02 per cent. of methyl alcohol. Some methylated ethers approach this very closely, although on the whole they are distinctly higher. That the impurities responding to this test are not the same in each specimen of ether is seen by the different behavior after extraction, first with alcohol and then followed by water. Some ether was taken and washed with

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5 Cc. of 10 per cent. alcohol, which was separated. Two further washings were rejected, but the fourth reserved. It was then further washed with two lots of 5 Cc. of water, the second lot being reserved for the test. The results are shown in the table, quantities being Cc. methyl alcohol.

Sample.	10 % Alcoholic Extract.		Aqueous Extract.
	1 st	4th	2d
Rectified	.001	.0002 (say)	nil
Meth. (boiling point)	.0015	Very faintly blue nil	nil
Meth. (low boiling point)	.0015	.0006 (say)	.002
Meth. (low boiling point)	.0025	.0004 (say)	.001

And if two portions of the same sample of ether be extracted, one with 10 per cent. alcohol and the other with water only, and the test applied, the difference between the two results varies with different makes of ether—the aqueous extract from one ether may give twice as strong an indication as the alcoholic extract, while with another ether it may be six or even more times as great. Of course, the effect in aqueous solution is not to be compared with that in the 10 per cent. alcohol, on account of the increased oxidizing power of the permanganate where the alcohol is absent.

But the experiment shows that while with some samples there are impurities extractable by alcohol, leaving no other oxidizable bodies behind, yet with others we may have the same impurities and further traces of other oxidizable substances as well. In short, the impurities vary with different ethers.

Rather than attempting any method of overcoming the inherent "ether effect" in this test, and bearing in mind the possibility of variation in its behavior in different hands, it is suggested that comparison against a given standard is much better than demanding a negative reaction. Such a procedure not only has the obvious advantage of being definite, but also ensures the proper working of the test, and gives evidence at once if the reagents are insufficiently sensitive. Probably a limit of an apparent 0.05 per cent. of methyl alcohol would be quite fair for a modern purified ether from methylated spirit. As to other impurities, since they are not specially guarded against in the Pharmacopœia, one may assume that such as occur in the usual course of events are not considered objectionable from the medical point of view. But the finding of the trace of formaldehyde in a sample of rectified ether which had been in stock

somewhat over a year, emphasizes very clearly the absolute necessity of the proper storage of ether and the desirability of not holding stocks too long. On one occasion, however, when requiring a very pure ether for some manufacturing purpose, it was thought desirable to estimate the amount of acetone or ketone present. The results are given in the table, and speak for themselves. Acetone is of fairly constant occurrence in methylated ethers, but one or two makers produce an ether of such purity as to give an all but negative reaction with the nitroprusside test. For the determination an adaptation of Scott-Wilson's method was employed, and, for the purpose of comparison, was quite satisfactory, although not exactly precise as here used. But I believe, by a little further development, it is capable of consistent accuracy when applied to ether.

Experimental.

The distillation was made with 100 Cc. of the ether in a three-bulbed Ladenburg flask connected with a small worm condenser, and using a standardized thermometer. A few pieces of pumice were placed in the flask. The correction for temperature was about 0.05 of a degree, and was, therefore, negligible. The source of heat was a small water bath, the cover having a hole cut in the center so as to expose only a small section of the bottom of the flask. *Methyl Compounds Test.*—A slight modification of the B.P. procedure is adopted for this test. The Schiff's reagent is prepared by powdering 0.5 Gm. of fuchsin and digesting with 90 Cc. of sulphurous acid (B.P.) overnight, by when it should be decolorized, then adding water up to 250 Cc. and filtering. For the test 5 Cc. of the ether is shaken up with 5 Cc. of a 10 per cent. mixture of absolute alcohol with water, and, after separating, drawn off into a boiling-tube.

For comparisons a dilution of 1 Cc. of pure methyl alcohol in 500 Cc. of water is made, so that each half of a Cc. represents 0.001 Cc. of methyl alcohol. A series of three test-tubes, similar to the above, are taken, and 0.5, 1.0, and 1.5 Cc. of the dilution run in, followed by ½ Cc. of absolute alcohol, and then 4½, 4, and 3½ Cc. of water added respectively, to make a total of 5½ Cc., which is approximately the volume of the ether extraction. The B.P. test is now followed, but, after adding the 5 Cc. of Schiff, each tube is thoroughly stirred with a thermometer, and carefully brought to a temperature between 45° and 50° C. The test is then set aside

until it has gained room temperature, or, preferably, for an hour. Under these conditions the test has given very satisfactory results. The reason for adopting this procedure was the experience that, with a *freshly-made* and *sensitive* Schiff, a bluish violet coloration was always obtained that was very confusing, no doubt due to acetaldehyde, and which would vary from time to time. But it was noticed that by heating as suggested this color would suddenly disappear at about 45°, and then the color due to the formaldehyde asserts itself. With 0.001 Cc. of methyl alcohol it requires about a quarter of an hour, but with 0.003 Cc. the color asserts itself almost as soon as the last trace of the fallacious coloration has disappeared. As thus set out the test makes comparison of an "apparent" 0.02, 0.04, and 0.06 per cent. of methyl alcohol in the 5 Cc. of ether.

One cannot urge too strongly the desirability of running the controls every time a test is made. There are too many variables influencing the test for one to rely solely on judgment of coloration.

Alkaline Silver.—A little 2 per cent. silver nitrate is added to an equal volume of caustic soda solution (20 per cent.) and cleared by the addition of just sufficient ammonia. Very pure ethers when shaken with this—say about 5 Cc. with 3 Cc. of reagent—give very little reduction indeed; on setting aside for five to ten minutes some samples are all but negative in reaction.

Formaldehyde may be detected by the usual gallic acid ring test.

Acetone.—This may be detected qualitatively by applying Rothera's modification of the nitroprusside reaction as described by Finnemore (*P. J.*, 25/7/14, pp. 139 and 160). Scott-Wilson's method[3] consists in precipitating the acetone or ketone as the mercury compound $HgC_3O(HgCN)_4$ by reacting with an alkaline silver-mercury cyanide solution and determining the mercury in the precipitate. It is an exceptionally delicate reaction, and one must always be careful to have an *excess* of reagent. In making qualitative tests nothing is easier than to achieve a negative indication through taking too much acetone. Alcohol does not appear to have any influence in small quantity, but aldehyde reacts after the manner of acetone, and ammonia, if present would also interfere. The reagent is prepared by dissolving 5 Gm. of mercuric cyanide and 90 Gm. of caustic soda in 600 Cc. of water, then 1.5 Gm. of silver nitrate in 200 Cc. of water, and gradually pouring this solution into the former under constant stirring. The reagent is then set aside to

[3] *Journ. Physiol.*, 1911, Vol. 42, 444.

deposit and become a brilliant solution. An acid mixture consisting of 40 Cc. nitric acid, 5 Cc. sulphuric acid, and 55 Cc. of water is required for dissolving the precipitate, and a standard solution of sulphocyanide, of which 1 Cc. will be equivalent to 1 Mgm. of mercury (about 1 Gm. KSCN per liter). The adaptation used is as follows:—1.08 Gm. of mercuric oxide is taken, mixed with a little water, dissolved by the aid of nitric acid, and then diluted to a liter —1 Cc. is equivalent to 1 Mgm. Hg. Twenty-five Cc. of this solution are mixed with 15 Cc. of the "acid mixture" and 2 Cc. of a saturated solution of iron alum, and then titrated with the sulphocyanide solution; a reddish-brown tint marking the end point. The value of the sulphocyanide in terms of mercury is thus obtained by a simple calculation. It is to be remembered that the presence of chlorides would vitiate this reaction.

In testing rectified ether 8 Cc. may be taken, but with methylated only 4 Cc., and with ordinary 720 methylated (not purified) 2 Cc. is sufficient. About 75 Cc. of distilled water is taken in a 100 Cc. graduated flask, and 10 Cc. of 2 per cent. silver nitrate solution, the ether is added, and the whole shaken till it is dissolved; 2 Cc. of 20 per cent. caustic soda solution are now run in, and the volume adjusted to 100 Cc. The flask is stoppered, inverted once or twice, and set aside for a minute or two; it is then vigorously shaken continuously for three minutes and then filtered. This treatment removes the aldehyde. The shaking is very necessary as otherwise traces of silver remain in colloidal suspension. Fifty Cc. of the reagent are placed in a conical flask, and then 75, 50 or 25 Cc. of the ether filtrate added according to the supposed contamination, but having rather *less than* 2 Mgm. of aectone to the 50 Cc. of reagent. The contents of the flask are thoroughly mixed, and a strong white turbidity appears within a second or two if any quantity of ketone is present. The flask is set aside over night, and in the morning the clear supernatant liquid carefully poured off under suction through a Gooch crucible which carries a moderately thick mat of pulped filter paper. (Whatman's 41 answers very effectively.) The precipitate is then washed on to the filter, and thoroughly cleansed with water till free from alkali. The filter mat and precipitate are then transferred to the original flask, disintegrated in a few Cc. of water, and then treated with 15 Cc. of the acid mixture and 2 or 3 Cc. of $\frac{N}{10}$ permanganate to help in the oxidation. The flask is either set on the steam bath for a quarter of an hour, or boiled for one or two min-

TABLE OF ANALYTICAL RESULTS.

Distillation Temperature, 100 Cc. Taken.	Samples from Industrial Spirit, Quantities in Cubic Centimeters.							Samples from Rectified Spirit.		
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
°C.										
Below 29°	10	—	—	—	—	—	—	—	—	—
29–30	13	—	—	—	—	—	—	—	—	—
30–31	14	20	—	—	—	—	—	—	—	—
31–32	14	15	15	—	—	—	—	—	—	—
32–33	14	16½	22	—	—	—	—	—	—	—
33–34	17	17	25	28	—	—	95	1	1	—
34–35 } B.P. {	14	18½	27	68½	97	97	2	69	94	—
35–36 } limit. {	—	8	7	—	—	—	—	21	1	—
36 and over	—	—	—	—	—	—	—	5	—	—
Recovery	96	95	96	96½	97	97	95	96	96	—
Methyl compds as "apparent" CH_3OH per cent.	0.03	0.05	0.05	0.05	0.03	0.06	Less than 0.02	Less than 0.02	0.08[4]	Less than 0.02
Pot. iodide test	Colorless	Straw	Just seen	Straw	Colorless	Colorless	Colorless	Strong lemon	Colorless	—
Caustic potash	In all samples a negative reaction									
Specific grav.	.7195	.7187	.7182	.7202	.7200	.7203	.7211	.720	.7207	.720
Tests other than B.P.										
Alkaline—silver	Black cloud, but transparent	Very slight	Nil.	Black, nearly opaque	Very slight	Slight	Slight	Very strong reduction	Negligible	—
Formaldehyde	Suspicions	Nil.	Nil.	Nil.	Nil.	Nil.	Nil.	Distinct reaction	Nil.	Nil.
Nitroprusside test (acetone)	3 min.	Nil.	5 min.	1 min.	1 min.	3 min.	½ min.	Nil.	Nil.	—
Ketone calculated as acetone in parts per 10,000	1.8	—	0.8	5.0	4.4	3.1	7.5	0.43	0.18	0.09
	(A sample of ordinary 720 "Industrial" ether showed 23.8 parts.)									

Sample 8 had been in stock for over a year.

[4] The methyl reaction could not be explained. This was a small sample specially obtained. These two rectified samples are given because of the abnormalities, formaldehyde and methyl compounds. In the nitroprusside test the time is that required for an unmistakable coloration to occur after adding the amount and well shaking up.

utes over a flame, to decompose and dissolve the precipitate. Care must be taken to see that the whole is taken up; with the larger quantities particles sometimes remain persistently insoluble unless rubbed down with a glass rod. The solution becomes colorless, and, after cooling, is titrated with the sulphocyanide as already described, using the iron alum as indicator. A deduction of 0.1 to 0.2 Cc. may be made for the amount required to give a satisfactory end point, but each experimenter should determine this for himself.

Each milligram of mercury represents 0.058 Mgm. of acetone. The following trials were made. A dilute acetone solution was prepared and its apparent strength determined by taking 10 Cc. together with 40 Cc. of water, and 50 Cc. of the reagent.

Determinations were then made by taking 4 Cc. of an ether and different quantities of the acetone solution, and proceeding as described above for the ether test. After making the necessary deduction for the "blank" of the ethers, the results were as follows:

Acetone Taken. Milligrams.	Acetone Found, Milligrams.	Deviation.
0.46	0.516	+ 11%
0.874	0.893	+ 2%
0.92	0.986	+ 7%
1.84	1.91	+ 4%
2.76	2.65	− 4%

Fifty Cc. each of reagent and filtrate being used. It will be noticed, consequently, that in the last test the reagent is insufficiently in excess for the quantity taken. These results were considered good enough for the comparisons desired, and the estimations were proceeded with. But it is believed that for absolute accuracy it would be necessary to keep to a fixed ratio of reagent to solution, and prepare a scale for different acetone concentrations.

This work was done in the Liverpool Laboratory of Messrs. Evans Sons, Lescher and Webb, Limited.

SOME PROPERTIES OF THE FAT-SOLUBLE VITAMIN (FAT-SOLUBLE A).[1]

The day has passed when even the most skeptical critic of novel hypotheses can deny that certain natural fats, notably milk fat, egg-yolk fat and various tissue oils, exhibit a peculiar potency in nutrition that is not shared by many other wholesome fats which enter into the dietary. Whether the property referred to be designated as a vitamin, a food accessory substance, a food hormone or auximone is of secondary interest so long as its chemical nature and mode of action are still so obscure. The fundamental fact that has been firmly established: When a suitable source of the fat-soluble vitamin as it exists either in animal fats or in green plants is lacking in the diet, nutritive disaster is certain to follow sooner or later, even when all other components of the ration are ideally adequate. We are here dealing with some as yet unidentified food factor indispensable for nutritive well-being, even though the quantity that is required may be measured with small units.

The earlier studies of the fat-soluble vitamin were largely directed to the search for its sources, so that it is now possible to catalogue a considerable list of foods of known potency with respect to the factor under discussion. The practical significance of this will be clearer to the medical practitioner when the bearing of a deficiency of fat-soluble vitamin on the genesis of certain symptoms of malnutrition is further elucidated. A shortage of the vitamin in the human dietary has already been convincingly related to the appearance of eye disease (xerophthalmia) in children; and English investigators are inclined to ascribe rickets to a similar deficiency factor. During the enforced food shortage of war-time days, the lack of butter, eggs and meats caused considerable concern to the food authorities. We have already pointed out that butter substitutes which are made from beef fats or oleo oils may be physiologically comparable to some extent with butter in their growth-promoting power, whereas those prepared from vegetable oils are inadequate in this respect.[2]

[1] From *Jour. Amer. Med. Assoc.*, Oct. 4, 1919.

[2] Osborne, T. B., and Mendel, L. B.: *J. Biol. Chem.*, 20: 379 (March), 1915. Drummond, J. C., and Halliburton, W. D.: *J. Physiol.*, 51: 235 (Sept.), 1917. Steenbock, H., Kent, H. E., and Boutwell, P. W.: *J. Biol. Chem.*, 35: 517 (Sept.), 1918. "A Problem Concerning Edible Fats," editorial *J. A. M. A.*, 69: 1876 (Dec.), 1917.

As might be expected, these pioneer studies of distribution are being followed by investigations of the properties of the unique something known as fat-soluble vitamin. It has not been identified with any of the recognized components of fats, such as glycerol, fatty acids, cholesterol, phosphatids or lipochromes. Several investigators, of whom the latest is Drummond[3] of the Cancer Hospital in London, have called attention to the ready destruction of the fat-soluble accessory food factor (*A*) after relatively short exposure to a temperature of 100° C. (212° F.). Longer exposures at lower temperatures, for example, 37° C. (98.6° F.) may be equally detrimental. This destruction is apparently not a result of oxidation or hydrolysis. The facts just cited render it impossible at the present state of knowledge to "harden" liquid oils, as is now so commonly done in the industries, without effecting a loss of the fat-soluble vitamin which the original fats may contain. This explains, further, why it is that the popular commercial hardened oils are devoid of the vitamin, whatever their origin may have been.

The specific rôle of the fat-soluble vitamin within the organism still remains unknown. The fact that it is found in certain fat depots of the body has suggested that it may play a part in the utilization of fats. Recent observations by Drummond[4] indicate that this is not the case, however. A deficiency of fat-soluble *A* in the diet does not exert any direct influence on the absorption of fat; and animals are able to absorb large amounts of fatty acids and presumably synthesize these into fats, in the absence of the fat-soluble vitamin.[5] Drummond[3] ventures to suggest that the latter is not a clearly defined chemical substance, but rather a "labile substance perhaps possessing characteristics resembling those of an enzyme." We shall await further investigations without the bias of a fixed hypothesis.

[3] Drummond, J. C.: "Researches on the Fat-Soluble Accessory Substance, I, Observations on Its Nature and Properties," *Biochem. J.*, 13: 8 (May), 1919.

[4] Drummond, J. C.: "Researches on the Fat-Soluble Accessory Substance, II, Observations on Its Rôle in Nutrition and Influence on Fat Metabolism," *Biochem. J.*, 13: 95 (May), 1919.

[5] "Fatty Acids as Foods," editorial *J. A. M. A.*, 73: 608 (Aug. 23), 1919.

NOTE ON THE QUANTITATIVE B.P. TEST FOR SODIUM SALICYLATE.[1]

By J. B. P. Harrison, F.I.C., and F. E. Carter, B.Sc.

The monograph of the British Phamacopœia states that sodium salicylate must contain 99.5 per cent. of the pure salt.

The quantitative test, as given in the paragraph headed "Characters and Tests," is thus described: "*2* Gms. heated to redness till gases cease to be evolved leave an alkaline residue which, when treated with water, filtered, and well washed, yields a clear solution requiring for neutralization not less than 24.8 milliliters of N/2 *solution of sulphuric acid.*" This is practically the same test as that prescribed for quantitatively determining sodium and potassium tartrate, but whereas in this instance very accurate results can be obtained, in the case of sodium salicylate varying results are given by different experiments on the same sample.

F. H. Alcock,[2] in a paper entitled "Sodium Salicylate," has drawn attention to this anomaly, and attributed the unsatisfactory results obtained by titrating the alkaline solution after treating sodium salicylate in the manner above described to the retention of part of the alkali by the carbonaceous matter which is filtered off, even after this has undergone very considerable washing with distilled water. This fact we can fully confirm, and at the end of this note shall give results in confirmation. Alcock, however, did not concern himself with improving the details of the method, but put forward a new process based on the decomposition of sodium salicylate by ammonium chloride when the two are heated together in strong aqueous solution.

One of the disadvantages of the alkalimetric process as described in the B. P. is that the solution obtained for titration with standard acid is often deeply colored with carbonaceous matter, so that it is difficult to see the change in color of the indicator at the end of the reaction. This tendency to produce a solution of colloidal carbon can be obviated in two ways. Firstly, by prolonged ignition of the carbonized mass whereby the carbon is either burned away or rendered in a form denser than that of colloidal carbon. In thus heating, however, there is a danger of raising the temperature of the

[1] Reprinted from *The Pharm. Jour. and Pharmacist,* Sept. 13, 1919.

[2] *P. J.,* Fourth Series, Vol. 23, p. 597.

mass higher than that at which the alkali melts, and so losing small traces by volatilization. Secondly, by neutralizing the alkaline solution with acid, the colloidal carbon is precipitated so that, on filtering, a clear water-white solution is obtained. This is the method proposed by Warington[3] in his classic papers on the analysis of commercial compounds of citric acid and tartaric acid, and with slight modifications is the official method for the assay of alkali salts of organic acids of the Ninth Decennial Revision of the United States Pharmacopœia, from which the following extract is taken: "After allowing the carbonized mass to cool, disintegrate it with the aid of a stout glass rod and transfer the mass and crucible to a beaker. Add 50 Mils. distilled water and 50 Mils. N/2 H_2SO_4, cover the beaker with a clock glass and boil for 30 minutes. Then filter the solution and wash the residue until the washings cease to redden litmus paper. Now determine the residual acid in the cooled filtrate by titration with N/2 KHO, using methyl orange as indicator."

In the case of sodium salicylate, low results are obtained by this method also, the carbon retaining a small portion of the alkali even after prolonged boiling with excess of standard acid. Warington has also stated that under some circumstances the charcoal retains a little acid, so that low results also would be caused by this effect.

To obviate these errors we have devised the following method, which gives very accurate results: About 1.5 Gm. are heated to dull redness till gases cease to be evolved, taking care not to fuse the carbonized residue. Detach the cooled mass from the crucible as far as possible by means of a glass rod and transfer to a beaker. Boil gently with 50 Cc. distilled water for at least five minutes, and pour the alkaline solution through a filter paper, keeping back as much of the carbon as possible. Boil again with more distilled water, transfer the whole to the filter and wash thoroughly with distilled water. After draining transfer the filter-paper and carbonaceous residue to the crucible, and ignite at a dull red heat until the carbon has been burned completely. Dissolve the residue thus obtained in water and add the solution to the filtrate already prepared. Now add excess of standard acid (say 50 Cc. N/2 H_2SO_4), cover with a clock glass, and heat the whole to boiling. In this way any colloidal carbon discoloring the solution is precipitated. Filter again, wash with hot distilled water until the washings cease to

[3] *J. C. S.*, 1875, 925–994.

redden litmus paper. Titrate the unneutralized acid with N/2 NaHO, using methyl orange as indicator. Each Cc. N/2 acid neutralized corresponds to 0.08 Gm. sodium salicylate. The following results show the relative merits of the methods above discussed:

(*a*) 1.6 Gm. analyzed by the B. P. method required 19.5 Cc. N/2 H_2SO_4, indicating only 97.5 per cent. sodium salicylate. A further 0.4 Cc. N/2 H_2SO_4 was used to neutralize the alkali obtained from the carbon residue, making a total of 99.5 per cent. sodium salicylate.

(*b*) 1.58 Gm. were examined by the U. S. P. method; 19.3 Cc. N/2 H_2SO_4, were neutralized by the alkaline solution, indicating 97.75 per cent. sodium salicylate; a further 0.3 Cc. N/2 H_2SO_4 was consumed by the alkali retained by the carbon residue, making a total of 99.25 per cent. sodium salicylate.

(*c*) 1.5885 Gm. were examined by the new process described; 19.75 Cc. N/2 H_2SO_4 were neutralized by the alkaline solution, corresponding to 99.44 per cent. sodium salicylate.

Experiments (*b*) and (*c*) were performed on portions of the same sample.

We are indebted to Messrs. Howards and Sons, Ltd., in whose laboratories the experimental work of this note was carried out, for permission to publish these results.

PRODUCTION AND EXPORTATION OF MERCURY IN SPAIN.[1]

By Trade Commissioner W. M. Strachan, Madrid.

Mercury is produced in the Provinces of Ciudad Real, Granada, and Oviedo, but the most important mines are those of Ciudad Real, which are located at Almaden and cover a surface of 485,187 acres. They are owned and operated by the state.

The Estadistica Minera de España contains some interesting statistics as to the cost of operation of the Almaden mines during the year 1917. In this year excavations were made at 300 sites, at which 2,765 cubic meters were excavated at a total labor cost of $97,333. The average daily wage paid was $2.50. The average labor cost per cubic meter was $35.20. The archwork, solid walls, and masonry

[1] From *Commerce Reports*, August 18, 1919.

erected for the interior support of the mines cost, for materials and labor, including transportation, timbers used for bracing galleries and shafts, etc., a total of $155,477. Shop expenses for work not let out by contract amounted to $15,931; the various articles classed as accessories cost $81,658, and labor not otherwise specified added $44,498 to the expense.

For labor used in distillation during 1917 the expenditure was $76,132, and for supplies $82,148. Ten pairs of Bustamente subliming furnaces, two Cormak-Spirek continuous-movement furnaces for fine materials, and three double-pan furnaces of the same system for coarse ores were employed. In the Bustamente furnaces 7,550 tons of mineral were treated, from which were produced 984,486 pounds of mercury. In the Spirek system 688,795 pounds of mercury were produced from 5,616 tons of ore.

Output and Quantities Exported.—The ore on hand at the beginning of 1918 amounted to 60,225 short tons and the production during the year was 11,013, making a total of 71,238 tons. Mineral treated during the year totaled 13,166 tons, yielding 911.7 tons of mercury; thus the metal content was 6.93 per cent.

The exports of mercury from Spain for the years 1908 to 1916, inclusive, were:

Year.	Pounds.	Year.	Pounds.
1908	2,353,629	1913	2,746,386
1909	3,069,959	1014	2,099,978
1910	2,466,935	1915	2,694,394
1911	3,293,392	1916	1,752,538
1912	2,769,085		

A comparison of the figures of output and export shows that practically the entire production is exported—chiefly to Great Britain.

PHARMACY IN THE RUSSIAN ARMY.[1]

Not the least interesting of many and varied experiences of pharmacy in war on many fronts has been work in Russia, where elements of old Imperial army were operating, side by side, with British units. During the dim days of an Arctic winter one has somewhat exceptional opportunities of studying the details of the pharmaceutical service of another army. The close relations recently existing between the medical service of the British and the Russian (pro-Ally) forces was nothing new, as the British medical profession has always been highly esteemed in Russia.

Historical.

So far back as the sixteenth century, and especially during the reign of Ivan the Terrible, English apothecaries were employed at the Imperial Court and held important positions among the Russian noblemen and statesmen. Queen Elizabeth was responsible for sending out the best known of these pioneers—James Roberts, who is still remembered under the name of "Jakobi." Waliszewski refers to this invasion of Russia by British doctors in his "Life of Ivan the Terrible" (translated by Lady Mary Lloyd). He says that "The whole of these foreign apothecaries could not have induced any native-born Russian to swallow a pill or accept any similar remedy. The moment a Muscovite felt out of sorts he drank a glass of vodka, seasoned with pepper or garlic, ate a slice of lemon, and took a clyster. This was his treatment for every complaint." Notwithstanding this, British medical men established themselves very successfully in Russia at this period and played an important part in its medical and pharmaceutical history during three centuries. The physicians and apothecaries retained by noble families were held in high honor and richly paid for their services. When they succeeded in effecting cures, estates, serfs, horses, and furs were bestowed on them with truly Oriental munificence. At the beginning of the seventeenth century a state dignitary with the title of *Apothecary boyar* was created, and, with the advent to power of the Romanoffs, the Tsar Michael instituted a pharmaceutical council. This council was an influential body, and appears to have controlled the practice not only of pharmacy but medicine

[1] Reprinted from *The Chemist and Druggist*, September 27, 1919.

as well. The Russian Army of this period was a remarkable body. It consisted chiefly of professional soldiers or musketeers, who lived in a special suburb of Moscow called after them. These musketeers followed various trades in peace time, but received subsidies from the Court and brought up their sons as hereditary soldiers of the Tsar. Like all privileged classes, they became inefficient and mutinous, and were ruthlessly wiped out by Peter the Great, who established an army and an Army Medical Service on the European model. The pharmaceutical council became the medical council, and a State Department under a Scotsman named Erskine, who was the Tsar Peter's personal physician. Owing, no doubt, to the influence of Dr. Erskine, Peter the Great spent large sums in the importation of medical and pharmaceutical educational material and in the equipment of hospitals and schools of medicine and pharmacy. In Peter the Great's army there were two apothecaries on the staff of every general, corresponding to our divisional commanders, and each division had two dispensaries, one for cavalry and one for infantry. Each dispensary had an apothecary-in-charge, with two apothecary's assistants and four pupils to assist him. There were also field hospitals for each division, and each had a field dispensary under the charge of apothecaries. After the death of Peter the Great pharmacy and medicine passed through many phases, and had numerous "ups and downs" until, at the beginning of the nineteenth century, the medical service of the army had been organized into a definite military department, with another Scot, Sir James Wyllie, at its head. Even Wyllie's influence, which was great, was not sufficient, however, to prevent the dual control of hospitals and dispensaries that had crept in during the period between the death of Peter the Great and the accession of the Tsar Paul. In Wyllie's organization was founded the position which still obtains—directors or commissaries of hospitals who are combatant officers, and directors of medical service who are medical men. The former are in charge of all economic and disciplinary matters, whereas the latter are merely responsible for professional and technical duties. On paper the organization of the Russian Medical Service during the Crimean War was excellent, but, like our own, it broke down completely during that campaign. The experience gained, however, led not merely to radical changes in the Russian Army as a whole, but also to a peaceful revolution in the

Russian national life. Serfdom was abolished and national service introduced. In 1869 comprehensive changes were carried out, and the system adopted which was found in Russia at the outbreak of war, and which has continued up to, and since, the revolution. Imperial Russia had the principle of universal service, but certain classes of the community, including doctors and apothecaries, were exempt from service with the Colors in peace-time. Society in Imperial Russia was divided into some fourteen classes. Each class had a definite position in the general community, and all who were government servants were entitled to wear a uniform. Russian officers of combatant services were the dominant class, and the term *ofitser* was actually reserved to them. Officials of the administrative services were not officers, but held in society the position accorded to their relative military rank. The Russian *brach* (surgeon) or *farmatsevt* (pharmacist) held precisely the same position in the Russian army as that occupied by surgeons and apothecaries in our own army prior to 1880. They had medical titles, and relative—but no actual—military rank or powers of command.

The Russian Army Medical Service.

In Russia the Army Medical Service includes the veterinary service, and not only are medical and veterinary stores kept in the same depôts but an actual interchange of duties was permitted, to some extent, between veterinary and medical *personnel!* There is not a special medical corps as in our own and most Continental armies, yet Russian war establishments before the war provided for 3,200 medical officers, 3,800 pharmacists, and over 52,000 medical rank and file. Several writers on the Russo-Japanese War, and on the earlier stages of the Great War, commented on the very generous provision of Red Cross *personnel* with Russian field armies, yet this large body of officers and men had not even a distinctive name and was largely composed of *personnel* temporarily detached from combatant units and other branches of the army. The Russian Medical Service—if we can use the term "Service" for such a heterogeneous staff—was composed of three elements: (1) Military medical *personnel;* (2) military non-medical *personnel;* and (3) civilians.

Military Medical Personnel.

The medical *personnel* consisted of: (*a*) Medical officers; (*b*) pharmacists; and (*c*) subordinate medical *personnel* (*feldshers* and *nadzirateli*). All surgeons in the Russian army are qualified medical practitioners before entering the army. They are classified in six grades, which correspond with the civil official rank as follows:

Medical Grade.	Corresponding Official Rank.	Corresponding Military Rank.	Civil Title.
1st	Fourth	Major-general	Privy Councillor
2nd	Fifth	Colonel	Actual State Councillor
3rd	Fifth	Colonel	Actual State Councillor
4th	Sixth	Colonel	State Councillor
5th	Seventh	Lieut.-Col.	Court Councillor
	Eighth	Captain	Collegiate Councillor
6th	Ninth	Lieutenant	Collegiate Assessor

The civil titles conferred certain privileges and were used in official correspondence. All candidates for appointment as *vrach* had to be qualified medical men, but as there were three grades in medical graduates the academic standing of the individual determined the grade to which he was appointed. Persons who had obtained the minor degree of *lekar* were appointed to grade 6, with the rank of lieutenant, whereas those who had obtained the higher degree of M.D. or M.D. and S. (Doctor of Medicine and Surgery) were appointed to the official eighth class, with the rank of captain, and the high-sounding title of collegiate councillor.

Appointment of Pharmacists.

Only graduates in pharmacy of the army medical academy or of a Russian university were appointed to commissions in the army. A *farmatsevt* must possess the lower degree of "Provisor" on appointment, but in order to get promotion he must take his degree as Master of Pharmacy. There are four grades of pharmacist, as follows:

Pharmaceutical Grade.	Corresponding Military Rank.	Civil Title.
1st, Glavini farmatsevt	Colonel	State Councillor
2nd, Starshi farmatsevt	Lieut.-Colonel	Collegiate Councillor
3rd, Mladshi farmatsevt	Lieut. or Capt.	Collegiate Assessor
4th, Aptekarshii pomoshohniki	Warrant officer	*Nil*

The Russian military pharmacists are a highly-trained and scientific body of men. In their hands are placed the preparation, supply, care, and dispensing of medical supplies of all kinds, the supervision and charge of military medical store depôts, the charge of analytical and bacteriological laboratories, and of Government factories for the manufacture of surgical instruments and druggists' sundries. The pharmacist official performs only the higher branches of pharmaceutical and administrative duties. The actual dispensing and the bulk of the duties performed by the sergeant and corporal dispensers of our R. A. M. C. are performed by dispensary *feldshers,* a body of subordinates.

Feldshers.

The *feldsher* is a peculiar feature of the Russian army. The term is applied to the members of a recognized inferior grade of medical, veterinary, and pharmaceutical practitioners. They are found in both civil and military practice, and nothing quite like them exists anywhere except India, where there are two bodies of medical public servants who correspond more or less exactly with the Russian *feldshers.* There are (*a*) the former apothecaries and (*b*) the former hospital assistants. The first-named are now called assistant-surgeons and the latter sub-assistant-surgeons. Both are employed in civil as well as in military practice. Both are regarded as qualified to practise outside the army—the apothecaries among all classes and the hospital assistants among the native community. In the Russian army the *feldshers* are the professional assistants of both medical and pharmacist officers, and may take their place just as the assistant-surgeon in India often acts for an R. A. M. C. officer and the sub-assistant-surgeon for an officer of the Indian Medical Service. Medical and pharmaceutical *feldshers* in Russia are trained either before entering or while serving with the army. Only the first class is qualified for civil practice, and this class may be trained in a civil or military medical school. If trained in a military medical school he must serve one and a half years with the active army for each year of instruction received, and the *feldsher* course lasts three years. Appointments are made by district army medical inspectors, and the pharmacist *feldsher* on appointment gets the sonorous title of *mladshi aptechni* (*feldsher*). For the second class of *feldsher* soldiers from combatant units are

selected and trained in military medical establishments. *Feldshers* trained in these military hospitals are appointed to companies, squadrons, and batteries, and are junior to the *mladshi aptechni feldshers,* who are employed with higher military formations or in hospitals. *Feldshers* may rise to the rank of "acting officer," a grade somewhat inferior to that of second-lieutenant in our army, but the majority remain non-commissioned officers all their lives. The pharmacist *feldsher* in civil life has limited powers as to the sale of drugs and medicines and is almost exactly comparable with the registered druggist in Ireland.

Nadzirateli of Hospital Sergeants.

The *feldshers* in Russia, like the doctors and pharmacist officers, are only engaged on professional duties. They have no purely military duties to perform. In Russian military hospitals the duties of ward master and hospital sergeant are performed by special *personnel* called *nadzirateli.* Their relationship with medical and pharmacist *feldshers* is peculiar and complicated. They give way to *feldshers* in all professional matters, but are senior to them in all matters of discipline and military precedence. This is typical of Russia, where the representative of executive authority is always superior to the professional or technical official, however highly trained. The result was that a vast host of combatant officers were employed in command of hospitals and military medical formations of all kinds. They had complete control over supply, general management, and interior economy. In peace-time the doctors are barely allowed to treat their patients or the pharmacists to dispense their medicines *secundum artem,* but in war they are given strictly limited powers of command. A *mladshi vrach* when carrying out periodical courses of instruction was not even allowed to command the stretcher-bearers of his unit. A combatant officer was placed in command ostensibly to learn the stretcher drill, but really to prevent a mere *vrach* commanding troops on any form of parade. Under the Republican *régime* this has been entirely altered, and some of the highest military commands are held by doctors.

Hospital Rank and File.

Non-commissioned officers for medical formations are drafted from combatant units. As in all other Continental armies a sharp

line is drawn between hospital orderlies and stretcher-bearers. The former are trained in nursing duties, whereas the latter are trained only in first-aid. Subordinate *personnel* for work in pharmacies is specially trained and not employed on other hospital duties. In Russia the regimental system of medical work[2] is developed to the fullest extent, and every effort is made to cure a sick soldier in the regimental *lazaret* or hospital. Each little regimental hospital has a dispensary *feldsher* and usually a well-equipped and well-stocked pharmacy. Pharmacist officers do not serve with regiments in peace or war. They serve on the staff of directors of medical services, have charge of hospital dispensaries, and are employed in depôts of medical stores, laboratories, and factories of medical material. Before the war a certain number of pharmacists were selected for the study of military pharmacy in foreign countries. They were sent abroad at the government's expense, usually for a period of two years.

The Russian Army has three types of field ambulance—regimental, divisional, and brigade. In Continental armies a "regiment" corresponds to our "brigade," and a "brigade" means a group of regiments smaller than a division. The field ambulances are called *lazarets,* and each has one, or more, dispensary *feldshers* who performs all the pharmaceutical duties. Behind the *lazarets* are field-hospitals, which are like our stationary hospitals. Attached to these are field convalescent depôts, which have no counterpart in the British Army. Behind the field hospitals are field clearing commissions corresponding to casualty clearing stations. A pharmacist officer is attached to each field hospital. He has a large subordinate *personnel* of *feldshers* and pharmacy attendants, ranks as a captain, and has the disciplinary powers of a company commander. Sometimes field hospitals are massed together in groups, and the pharmacy is then a very big affair indeed, and the single pharmacist officer has a responsible charge. Pharmacist *feldshers* are employed in bacteriological and disinfection columns, but the pharmacist or his *feldsher* may be found everywhere. One of their most important functions is the care of the

[2] See "Pharmacy in the French and Italian Armies," *C. & D.,* June 7, p. 50, and June 14, p. 64.

Units for the Supply of Medical Equipment.

There are two classes of units corresponding to the British advanced depôts of medical stores—field dispensaries and temporary dispensaries. A temporary dispensary has no fixed establishment, whereas a field dispensary is under a *glavni farmatsevt,* ranking as a lieutenant-colonel with a captain as second in command, one to two junior pharmacists, and a large staff of *feldshers* and *attendants.*

A special feature of these field dispensaries is an instrument-repairing shop, with a foreman cutter and trained instrument repairers. Until the revolution the army medical factory at Petrograd was the most important and extensive of its kind in any country.

It consisted of a pharmaceutical laboratory, a surgical dressings mill, and a surgical instrument factory. The latter was in charge of a medical officer of the highest rank, with surgeon-colonels in charge of each section. The medical officers were, however, largely ornamental, and the real work of the factory was carried on by pharmacist officers.

The Red Cross.

Before the war the Russian Red Cross was perhaps the best organized and wealthiest of all the European Red Cross Societies. In addition to the usual private sources of revenue of such bodies it was heavily endowed by the State. The Society had the monopoly of the sale of picture postcards. It received a percentage tax on public and private entertainments, and also the revenue from the sale of stamps on railway tickets and of surcharges on telegrams.

It was very active in peace-time and carried out important relief duties, such as sending detachments to work among the Russian fishermen on the north coast of Norway and among the islands of the Arctic Ocean, but its chief work was the organization and maintenance of lay-communities known as the "Sisters of Mercy of the Red Cross." It employed a large number of pharmacists, as the Red Cross supplied practically every form of medical formation. The Red Cross units worked side by side with those of the regular medical service in the most forward positions. Pharmacists with the Russian Red Cross had all the privileges of their comrades with the regular army. Under the Republican *régime* the pharmacist

was admitted into the class known as the *intelligentsia,* which included all the professional sections of the community and, prior to the Bolshevist upheaval, had the complete control of the executive.

The whole of Russia's political, social, and economic life is now in the melting-pot. British influence was, as has been already shown, the greatest factor in developing the position of medicine and pharmacy in Russia during the past three centuries, and it will be interesting to observe what part will be played in the organization of these twin arts, in the future, by British pharmacy.

M.D., L. P. S. I. (69/91.)

PHILADELPHIA COLLEGE OF PHARMACY, MINUTES OF THE SEMIANNUAL MEETING.

The semiannual meeting of the Philadelphia College of Pharmacy was held September 29, 1919, at 4 P. M. in the Library, the president, Howard B. French, presiding. Twenty-four members were present, with regrets from Joseph L. Lemberger.

The minutes of the quarterly meeting held June 30 were read and approved. An abstract from the minutes of the Board of Trustees for June were read by the Registrar, J. S. Beetem, and approved.

Professor Charles H. LaWall reported verbally for the delegates to the meeting of the American Pharmaceutical Association held at New York City, August, 1919. The College was well represented by its faculty and members. Unquestionably it was a very successful meeting. A number of the members of the College were appointed to various committees, and Professor Lucius E. Sayre, an alumnus and member, was installed as the President.

Professor J. W. Sturmer for the delegates to the Conference of Pharmaceutical Faculties reported verbally that the Conference was somewhat unusual in that there were no "hot fights." One of the most important subjects discussed was that of Four Years High School Requirements for College Entrance—previously agreed upon to become operative September, 1923. A motion to require a four-year course earlier than 1923 was voted down; the other business discussed was mainly along technical lines.

Professor E. Fullerton Cook for the Committee on Nominations

presented the list of nominees for Trustees to be voted for at this meeting. In connection with the report a letter from Edwin M. Boring, one of the nominees, was read, requesting that his name be withdrawn because of physical debility. He had been a member of the Board of Trustees uninterruptedly for forty-one years, and he thought a younger man should be chosen. A number of the members spoke appreciatingly of Mr. Boring's services and hoped he would continue in the services of the College.

Professor Cook requested that the nominations be reopened, and this motion having been adopted another name was placed in nomination. Messrs. Leibert, Thum and Blackwood were appointed tellers. While the votes were being counted, Mr. George M. Beringer reported that the proposed amendments to the charter of the College were now being considered by the state authorities and it was expected that a favorable action would be reported.

Mr. Beringer alluded to the coming Convention to revise the United States Pharmacopœia and thought that we had overlooked the important part the College had always taken in the decennial revisions and suggested that a committee be appointed to present to the Convention in May, 1920, a report embodying the views of the College and recommendations for the revision. It was so ordered, and the president was authorized to appoint the committee.

Dr. A. W. Miller read abstracts from a communication from the University of Bonn, referring to some phases of education resulting from war conditions.

The Committee on Membership reported favorably on six applications for membership in the College. A ballot being taken they were unanimously elected, as follows: Virgil Coblentz, New York City; John G. Eby, Camden, N. J.; J. Howard Houck, Indiana, Pa.; John H. Miller, Lancaster, Pa.; Harold R. Waidelich, Allentown, Pa., as active members, and William G. Schmidt, Philadelphia, as associate member.

Dean Charles H. LaWall reported that up to this date the matriculants in the first-year class in the College numbered 280, the second-year class 160, with increased classes in the postgraduate courses and of special students. There were thirty-five women students enrolled among the number. These figures show a large increase in all the classes.

The tellers reported that Edwin M. Boring, Theodore Campbell

and Aubrey H. Weightman were elected as Trustees for the ensuing three years.

The President reappointed the Committee on Membership, as follows: Freeman P. Stroup, Frank R. Rohrman and O. W. Osterlund, with the Secretary and Treasurer, exofficio.

C. A. WEIDEMANN, M. D.,
Recording Secretary.

THE BEECHNUT PACKING COMPANY CASE AND ITS RELATION TO THE "COLGATE PLAN."

BY J. E. WALSH,
NEW YORK, N. Y.

The drug trade is probably very much interested in the general question of price maintenance and price cutting and more particularly in the Beechnut Packing Company case which will come up before the Circuit Court of Appeals probably at its next session.

It was generally supposed that the decision of the United States Supreme Court in the Colgate case determined once and for all the right of any manufacturer to refuse to sell his goods to a price-cutter which has come to be known as the "Colgate Plan" for the protection of resale prices. But this policy is once more the subject of litigation.

The decision of the Supreme Court was that this policy did not violate the Sherman Law. Since it was rendered, the United States Circuit Court of Appeals has decided, in the case of Frey *vs.* Cudahy & Company, that that sales method does not violate the Clayton Act. The Federal Trade Commission, however, claims that it does violate the provision of the Federal Trade Commission Act which prohibits "all unfair methods of competition." They assert that the maintenance of prices by the withholding of supplies from price-cutters is such an unfair method of competition.

The Commission accordingly entered an order against the Beechnut Packing Company, requiring it to desist from this sales policy. From that order the Company has appealed to the United States Circuit Court of Appeals, where the case is now pending. It will be argued on behalf of the Beechnut Packing Company by

Hon. Charles E. Hughes, who argued the Colgate case in the Supreme Court. The Beechnut Packing Company has announced that if the case goes against it, an appeal will be taken to the Supreme Court. Probably the Federal Trade Commission will take such an appeal, if the case goes the other way.

This case raises one entirely new question. The Beechnut Packing Company has extended the "Colgate Plan" and not merely does it refuse to sell to price-cutters, but it refuses to sell to dealers who are supplying price-cutters, even though these dealers may themselves adhere to the suggested price schedule. This additional step in price protection has never come before the courts. So far as this feature of the Beechnut sales policy is concerned, the question at issue is not only whether it violates the Federal Trade Commission Act, but whether it violates the Sherman Law. In so far as the right to refuse to sell to price-cutters is concerned, the only question at issue is whether such a refusal is contrary to the Federal Trade Commission Act. So far as concerns the right to refuse to sell to one who is in turn supplying price-cutters, there are two questions at issue, viz: The first, whether it violates the Sherman Law, and the second, whether it violates the Federal Trade Commission Act.

THE SKIN REACTIONS FOR TUBERCULOSIS.[1]

An exhaustive report on the value of the Moro and von Pirquet tests for tuberculosis is given by J. W. Allan (*Glasgow Med. Jour.*, 1918–19, 90–1, 321, 25; Dec.–Jan.). Moro's test consists in rubbing into a limited area of skin an ointment containing Koch's old tuberculin. Von Pirquet's test consists in the inoculation, through an abrasion made in the skin, of a solution containing Koch's old tuberculin. A large number of cases are described, the results presenting considerable variety, and the author concludes that slight or early cases give the best response. Advanced cases with pyrexia fail to give a reaction. Allan concludes in the following words:

"When we get a positive reaction in cases where the bacteriological report is negative, it is to be borne in mind that the failure to detect T. B. is not a conclusive proof that the patient is free from tubercle. The same applies to a negative result from auscultation

[1] Reprinted from *The Prescriber*, September, 1919.

and percussion of the chest. Even a skilled and experienced physician may fail to detect the lesion in a tuberculous lung.

"When we get a positive reaction we may conclude that the patient is affected with tubercle, but it is not necessarily active; it may be latent tubercle.

"The impression left on my mind by the application of these tests is that they are, on the whole, helpful aids to diagnosis. And these cutaneous tests have the advantage that we may use them without fear of doing harm."

DISPOSAL OF THE GOVERNMENT STOCK OF PHENOL.

An announcement of importance to the chemical, pharmaceutical and dyestuff industries has been made by the United States government concerning disposition of its large surplus of phenol.

Prior to the signing of the Armistice many millions of pounds of phenol were required by the War Department for the manufacturing of picric acid and other explosives.

As was to be expected the sudden termination of hostilities left an unprecedentedly large amount on hand. It was estimated the quantity was sufficient to cover the peace-time requirements of the United States for four years or more.

The result was a generally depressed market. Phenol being quoted freely much below actual cost without sales. It was a problem for the government to get rid of this great surplus without serious injury to the producers and with the greatest possible profit to the government.

To formulate plans and with the view of coöperating with the industries concerned, a meeting was called during the early part of April at the Chemists Club, New York City, which was attended by representatives of the various interested houses. Pessimism ruled. Many suggestions were made, among others that this vast stock be destroyed with the view of protecting the industry. Finally a representative of the Monsanto Chemical Works expressed faith in Phenol and its future, and gave the opinion that with the proper tariff protection of dyestuffs increased production would result, with a corresponding increased use of phenol.

While nothing definite resulted at the time of the meeting re-

ferred to, it was shortly followed by offers from the Monsanto Chemical Works to buy the entire amount at a price of several cents above the then prevailing market, or to act as the government's agent, thereby permitting the government to receive the benefit of any advance in price.

The War Department officials favored the latter plan, with the result that the Monsanto Chemical Works have received a contract making them sole selling agents for approximately 30,000,000 pounds of phenol.

BOOK REVIEWS.

THE CONDENSED CHEMICAL DICTIONARY: A reference volume for all requiring quick access to a large amount of essential data regarding chemicals and other substances used in manufacturing and laboratory work. Compiled and edited by the Editorial Staff of the Chemical Engineering catalog. Published by the Chemical Catalog Company, 1 Madison Avenue, New York. Price, cloth $5.00; leather-bound and thumb-indexed, $6.00.

The review of a reference book is a difficult undertaking. For proper appraisement of the value of a book of this class it must be used in actual practice over a long period of time.

The book, which was recently issued under the title given above, essays to be more than its name indicates, for it contains so many drug titles as well, that it might easily be termed "A Dictionary of Substances used in Medicine, Pharmacy and in the Sciences and Arts."

To give one who has not seen this book an idea of its comprehensiveness and accuracy can be done only by selecting some one subdivision or group of substances and comparing them with a corresponding list in some other authoritative work. In this case the acids were chosen as the group and the U. S. P. as the authority. On page 504 of the U. S. P. in the table of molecular weights there begins a list of about fifty titles of acids, not all of which, however, are official, either in the text or as reagents. The Condensed Chemical Dictionary lists the titles and descriptions of nearly 200 different acids of greater or less commercial importance and in addition contains more than 200 cross references.

The data given under each heading are of both scientific value and practical importance and are as follows: Physical properties, constants, solubilities, derivation, method of purification, grades, containers, uses, fire hazard and railroad shipping regulations. The information is given concisely yet intelligibly. So far as accuracy is concerned it is probably above the average book of its kind, no book ever published being perfect in this respect. For instance, the following errors were noted in this same group of acids that were selected for critical study and it may be assumed that the remainder of the book will show about the same degree of accuracy.

Under acetic acid, no mention is made of its use in pharmacy or medicine. Under some of the acids, "U. S. P. grade" is mentioned, although the U. S. P. makes no mention of this acid at all except perhaps in the table of molecular weights or under the reagents. Among these are bromic, aminoacetic, anthranilic, butyric, formic (official in N. F.), iodic, molybdic, monochloracetic, ortho-arsenic, oxalic, perchloric, phosphoric (anhydrous), phosphoric (glacial), phthalic, silicotungstic, succinic, sulphurous and valeric.

Under hydrocyanic acid the strength is mentioned as 10 per cent., a dangerous bit of misinformation.

Incorrect strengths are given for hydriodic acid and hydrobromic acid.

Under hypophosphorous acid the formula is incorrectly given as $H_3P_7O_2$.

If errors in the other parts of the book are in the same proportion, and quite a number were noticed which it is not necessary to mention, there would be upward of 200 errors in the whole work. This would not be a great number considering the number of titles involved. The errors noted were of minor importance in the majority of cases.

The work is well cross-indexed as regards the names and synonyms of crude drugs and fixed and volatile oils as well as chemicals.

The latter portion of the book is devoted to tables of atomic weights, weights and measures, equivalents temperature conversion tables, specific gravity tables and a list of definitions of units of measurements, many of which would be difficult to find except in highly specialized literature.

The transportation regulations are also fully outlined, both as regards freight and express matter.

The book will undoubtedly find a ready field and the future editions, which will doubtless be found necessary, will probably be free from the defects which usually attend the production of the first edition of such a work.

C. H. LAW.

REVISION OF THE NORTH AMERICAN SPECIES OF XANTHIUM. By Charles F. Millspaugh and Earl E. Sherff, Field Museum of Natural History, Chicago. Publication 204, Botanical Series, Vol. IV, No. 2.

In this splendid monograph the authors have apparently settled numerous matters of bibliography attendant upon North American species of *Xanthium*. A brief history of the work done on these plants by several investigators is first given. This is followed by the characteristics of the genus *Xanthium*, a key to the identification of the species considered, and the characteristics and distribution of twenty-one species. Accompanying the article are seven clear plates, four of which depict the fruit characters of numerous species, the remaining three, the characteristics of the fruiting plants of *Xanthium curvescens*, *X. calvum* and *X. australe*, respectively.

HEBER W. YOUNGKEN.